Impaired Learning of Phonetic Consistency and Generalized Neural Adaptation Deficits in Dyslexia

by

Tyler K. Perrachione

B.A. Linguistics and Cognitive Science
M.A. Linguistics
Northwestern University, 2007

SUBMITTED TO THE DEPARTMENT OF BRAIN AND COGNITIVE SCIENCES
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY
AT THE
MASSACHUSETTS INSTITUTE OF TECHNOLOGY

JUNE 2012

Signature of Author: _____
Tyler K. Perrachione
Department of Brain and Cognitive Sciences
April 9, 2012

Certified by: _____
John D.E. Gabrieli
Grover Hermann Professor in Health Sciences and Technology
and Cognitive Neuroscience
Thesis Supervisor

Accepted by: _____
Earl K. Miller
Picower Professor of Neuroscience
Director, BCS Graduate Program

Impaired Learning of Phonetic Consistency and Generalized Neural Adaptation Deficits in Dyslexia

by

Tyler K. Perrachione

Submitted to the Department of Brain and Cognitive Sciences
on April 9, 2012 in partial fulfillment of the
Requirements for the Degree of Doctor of Philosophy in
Neuroscience

Abstract

Developmental dyslexia is a neurological condition that specifically impairs the development of expert reading ability. Phonological processing deficits – impaired representation of, or access to, the abstract units of spoken language – have been implicated as the principal source of reading difficulties in dyslexia, independent of other cognitive factors. However, the source of these phonological impairments remains unknown: What mechanisms preclude development of the robust phonological representations critical for reading development? Experiments with phonological processing in dyslexia typically employ metalinguistic tasks that require explicit knowledge about phonological structure, failing to distinguish between access to representations and the representations themselves. Here I report a series of experiments that elucidate the nature of phonological impairments in dyslexia by examining the implicit processing of phonetic variability. Phonetic variability affects language processing at the interface between perceiving the physical speech signal and mapping it onto stored linguistic representations. This approach is well-suited to interrogate the integrity of phonological processing in dyslexia and to provide insight into how phonological representations may come to be impaired in this disorder.

In Experiment 1, individuals with dyslexia demonstrated profoundly reduced ability to learn to use phonetic consistency in talker identification, thus reifying the status of phonological representations themselves as fundamentally impaired in this disorder. In Experiment 2, functional magnetic resonance imaging (fMRI) adaptation revealed reduced neural sensitivity to phonetic consistency during speech perception in individuals with dyslexia, indicating impaired rapid, implicit learning of phonetic-phonological consistency. The neural mechanisms that support such learning may be a specific instance of general brain mechanisms for adapting to stimulus consistency. In Experiment 3, fMRI adaptation further revealed that such exiguous neural plasticity in dyslexia is not limited to speech phonetics; instead, the core mechanisms of rapid adaptation to stimulus consis-

tency appear to be dysfunctional in dyslexia, such that neural adaptation was reduced to all stimuli measured, whether auditory or visual, linguistic or non-linguistic. Deficits in neural adaptation may represent disruption of a core rapid plasticity mechanism for perceptual learning, dysfunction of which would impair the ability to develop the robust perceptual (phonological) representations critical to reading development.

Thesis Supervisor: John D.E. Gabrieli
Title: Grover Hermann Professor in Health Sciences and Technology and Cognitive Neuroscience

Acknowledgments

It has been a unique privilege to attend MIT and pursue a line of research I found extremely interesting, resulting in this dissertation. MIT and the Department of Brain and Cognitive Sciences have been a remarkable intellectual environment, and I am deeply appreciative of the people and resources that have helped bring life to my science. Foremost, I am extremely grateful for the guidance and support of my mentor, John Gabrieli, whose scientific insight and breadth of curiosity are inimitable. Patrick Wong, my former advisor at Northwestern University, has made an inestimable contribution to my development as a scientist, and I am grateful for my continued relationship with him. I am also extremely fortunate to have been able to work closely with Satrajit Ghosh, who has contributed so much crucial technical and scientific insight in support of my science.

I would like to thank the other members of my thesis committee, Stefanie Shattuck-Hufnagel, Nancy Kanwisher, and Bob Desimone for their time, support, and insightful discussion of this research. I would also like to thank Ted Gibson, Ken Wexler, and, especially, Chris Moore for many inspiring conversations during my graduate career.

The work presented in this thesis would not have been possible without the generous support of many other members of the Gabrieli laboratory, including especially Stephanie Del Tufo and Rebecca Winter, who conducted the vast majority of neuropsychological assessments reported here. Joanna Christodoulou, Marianna Eddy, Ioulia Kovelman, Eveline Geiser, and Sue Whitfield-Gabrieli provided invaluable discussion in the development of these and other projects during my graduate career. Additionally, Carlos Cardenas-Iniguez, Sara Beach, Dasun Peramunage, John Lymberis, Abigail Cyr, Sok Ee Lee, Elizabeth Norton, Bianca Levy, and Patricia Chang were instrumental in producing many of the data reported here. Thanks also to Cindy Gibbs for everything she has done to make our science possible.

I am very grateful to the Martinos Imaging Center at the McGovern Institute, and particularly Christina Triantafyllou, Steve Shannon, and Sheeba Arnold. I am also grateful to the faculty in the MIT Program in Speech and Hearing Bioscience and Technology, who have been so supportive of my education here: M. Chris Brown, Bertrand Delgutte, and Jennifer Melcher. Thanks also to Randy Gollub, Cara Stepp, and Adrian K.C. Lee.

My original introduction to the science of speech and language came from Bob Gundlach at Northwestern University, and I am deeply appreciative for the support of the faculty there whose early support and enthusiasm helped set me on my way in science: Janet Pierrehumbert, Matt Goldrick, Minjoo Kim, and Ann Bradlow.

Having reached the pinnacle of my formal education, I would like to thank the teachers at every level who helped bring me here: Jane Fouch, Diane Aldrich, Mary Ellen Bishop, Sarah Bowers, Bonnie Goodwin, Claire Jepson, Linda Hudnall, Susan Hazen, Mindy Thompson, Jim Kelly, Emil Helmich, Darwin Hartsock, Christie Taylor, Julie Minn, Yves Whitman, Judy Allen, Deena Berry, Tom Nothdurft, Jane Mauck, Karen Mulford, and Mary Grossnickle.

Lastly, I would not have been able to undertake any of these scientific or educational experiences without the lifelong kindness, support, and love of my family: my dad, who is my hero and inspiration, and whom I hope to be just like one day; and my mom, who is my first and greatest teacher. Thanks to Gwen and to my sisters, Courtney and Sara, for their love and encouragement, and to my grandparents, whose foresight and beneficence made it possible for me to attend university. Finally, thanks for everything to my wife Arim, because of whom I realize how lucky I truly am.

Table of Contents

Abstract....3
Acknowledgments....5
1. Introduction....11
1.1 Phonetic variability in speech perception....11
1.1.1 The cognitive costs of phonetic variability in speech perception....13
1.1.2 The benefits of phonetic variability for talker identification....14
1.1.3 The benefits of phonetic variability for speech learning....15
1.2 Phonological representations and learning to read....16
1.3 Developmental dyslexia and a phonological deficit....16
1.3.1 Whither speech perception deficits in dyslexia?....17
1.3.2 Non-reading perceptual impairments in dyslexia....18
1.3.3 Non-phonological theories of visual deficits in dyslexia....19
1.4 Dysfunctional neural adaptation as a framework for understanding the source of a phonological deficit....20
2. Phonologically-based voice recognition deficits in dyslexia....25
2.1 Introduction....25
2.2 Methods....28
2.2.1 Participants....28
2.2.2 Stimuli....29
2.2.3 Procedure....30

2.3 Results....31
2.4 Discussion....34
3. Reduced neural sensitivity in dyslexia to phonetic consistency in speech perception. .37
3.1 Introduction....37
3.2 Methods....38
3.2.1 Participants....38
3.2.2 Stimuli....39
3.2.3 Procedure....39
3.2.4 MRI Data Acquisition....42
3.2.5 MRI Data Analysis....42
3.3 Results....46
3.3.1 Task-related activation....46
3.3.2 Adaptation to the phonetic consistency of a single talker....46
3.4 Discussion....49
4. Generalized neural adaptation deficits in dyslexia....51
4.1 Introduction....51
4.2 Methods....54
4.2.1 Participants....54
4.2.2 Stimuli....56
4.2.2.1 Experiment 3a – Spoken Words
4.2.2.2 Experiment 3b – Written Words
4.2.2.3 Experiment 3c – Objects
4.2.2.4 Experiment 3d – Faces
4.2.3 Procedure....57
4.2.3.1 Experiment 3a – Spoken Words
4.2.3.2 Experiment 3b-d – Written Words, Objects, and Faces
4.2.4 MRI Data Acquisition....59
4.2.5 MRI Data Analysis....59
4.3 Results....61
4.3.1 Experiment 3a: Spoken Words....61
4.3.1.1 Task-related activation
4.3.1.2 Adaptation to repetition of spoken words
4.3.2 Experiment 3b: Text....63
4.3.2.1 Task-related activation
4.3.2.2 Adaptation to repetition of written words
4.3.3 Experiment 3c: Visual objects....65
4.3.3.1 Task-related activation

4.3.3.2 Adaptation to repetition of visual objects
4.3.4 Experiment 3d: Faces....68
4.3.4.1 Task-related activation
4.3.4.2 Adaptation to repetition of faces
4.4 Discussion....72
5. Conclusions:
A neural adaptation dysfunction framework for understanding the source of phonological deficits in dyslexia....75
References....81

1. Introduction

Learning to read is one of the most remarkable and complex examples of human learning. Unlike spoken language development, which proceeds naturally and spontaneously in human infants, learning to read requires lengthy, explicit instruction and comprises a major portion of early education. Successful reading development depends on the ability to learn the correspondence between a collection of arbitrary, invented visual symbols and the abstract phonological representations of auditory language. Some individuals experience disproportionate difficulty learning to read due to developmental dyslexia, a neurological condition that specifically impairs the development of typical reading ability. The principal source of reading difficulties in dyslexia is thought to be an impairment in phonological processing. However, the specific mechanisms that give rise to impaired phonological representations remain unknown. This thesis investigates the nature of impaired phonological representations in developmental dyslexia from the perspective of the interface between phonetics and phonology. In particular, we will consider the cognitive challenges posed by processing phonetic variability in speech perception and investigate how phonetic variability is learned in dyslexia, with an emphasis on working towards identifying a potential core neurobiolgical mechanism, dysfunction of which may plausibly contribute to to impaired phonological representations in dyslexia.

1.1 Phonetic variability in speech perception

Although we have the subjective experience of perceiving speech fluently and effortlessly, exceptionally complex computational processes are required to extract an unambiguous linguistic message from an immensely variable physical signal. Unlike the written symbols of language, which are highly homogeneous, the acoustic realization of

language is virtually never identical from instance to instance. The immense variability in the physical properties of speech is classically captured by Peterson and Barney (1952; see also Hillenbrand *et al.*, 1995), whose acoustic measurements of the vowels of English reveal seemingly irreconcilable overlap in phonological categories across talkers and tokens. Indeed, there exists a multitude of potential sources of acoustic variability in speech production, including anatomical and physiological differences among talkers, coarticulatory effects on the phonetic realization of speech, and culturally constrained differences in the diversity and prototypicality of speech sounds.

Differences among talkers result in a wide variety sources of variability in speech production. Differences in the volume, length, and shape of the oral, pharyngeal, and nasal cavities effect differences in resonance and thus differences in the local peaks and valleys of the speech spectrum. Differences in vocal physiology (and, sometimes, pathology) result in the wide range of factors collectively known as voice quality, including open quotient and harmonic ratio of the laryngeal source. Gender differences between talkers correspondingly result in substantial differences in speech acoustics: males tend to have longer vocal tracts and therefore lower frequency resonances, whereas the shorter vocal tracts of females result in higher formant frequencies. Differences in talkers' fundamental frequency (pitch) – both in terms of absolute value and dynamic range – have profound effects on speech acoustics, including especially the resolution of the speech spectrum. Moreover, patterns of speech and speech sounds are culturally constrained, and the particular diversity of speech sounds an individual may employ depends on the language, dialect, and accent they acquired as children.

Coarticulatory effects, likewise, have substantial impact on the acoustics of speech production. The phonetic features of sounds occurring in sequence are influenced by the place and manner of articulation of not only the sounds that immediately precede and follow them, but often in many cases by sounds that occur even distantly in the same or temporally neighboring words. Talkers may adopt different registers when speaking in different environments, and any number of exacerbating factors may affect the precision

of articulation, including especially speech rate or the presence of environmental noise. Given the multitudinous factors bearing on the acoustic realization of speech, it should come as no surprise that there is a quantifiable cognitive cost to processing variability in speech perception. Or, said another way, there is a great deal of computational economy to be gained by being able to construct predictive models in the presences of short-term consistency in speech phonetics.

1.1.1 The cognitive costs of phonetic variability in speech perception

That attending to the speech of a single talker affords both speed and accuracy benefits over processing speech from multiple different talkers has been demonstrated through a wide range of behavioral assays, including speeded classification tasks, continuous recognition memory tasks, speech in noise perception, auditory stream segregation, and phonological contrast learning. These experiments can be broadly divided into two kinds: those that show a processing cost for accommodating speech from additional sources, and those that show processing enhancement for encountering speech from a consistent, familiar source.

When listeners are required to make perceptual judgments about speech stimuli, they incur a processing cost as additional variability is introduced into the stimuli. For instance, Mullennix and Pisoni (1990) showed that listeners are slower to identify the initial phoneme in spoken words when recordings from multiple talkers are included in the stimulus set and faster when speech from only one talker is used. A corresponding effect was observed for making determinations about vocal identity, which was slowed as the phonetic diversity of the stimulus set increased. Similar results were obtained by Green, Tomiak & Kuhl (1997), who additionally showed that phonetic variability due to differences in speech rate could incur a similar cost.

Listeners are also faster and more accurate at speech memory tasks when the phonetic properties of words are more similar during encoding and recognition (Palmeri,

Goldinger, & Pisoni, 1993). When listening to speech in noise, listeners are more accurate at recognizing words if they have previously been familiarized with the talker who produced them (Nygaard, Sommers, & Pisoni, 1994), and listeners are better able to attend to one of two competing talkers when they are familiar with the talker's voice (Newman & Evers, 2007). These advantages appear to be due specifically to learning the properties of phonetic consistency from a target speech source; when these phonetic properties are changed, such as between words spoken in isolation or connected speech in sentences, the advantage is lost (Nygaard & Pisoni, 1998). Moreover, *only* manipulations that affect the phonetic properties of speech appear to give rise to such perceptual or memory advantages: Changing the talker or rate of speech reduces response accuracy, but merely changing its amplitude does not (Bradlow, Nygaard, & Pisoni, 1999). Finally, listeners' perceptual expectations about learned phonetic consistency appear to guide speech perception behaviors in real time (Creel, Aslin, & Tannenhaus, 2007; Allen & Miller, 2004; Theodore & Miller, 2010).

1.1.2 The benefits of phonetic variability for talker identification

Although variable phonetics may obfuscate the underlying linguistic content of an utterance, the fact that different talkers produce speech with largely idiosyncratic phonetics provides an additional source of highly informative cues to talker identity. We can be sure that listeners are using the phonetic nuances of individual talkers to help identify them from experiments that show reduced ability to recognize voices speaking a foreign language (Thompson, 1987; Goggin *et al.*, 1991). When trying to identify a voice speaking a familiar, comprehensible language, listeners can take advantage of the fact that they are also able to understand the linguistic content of the message. By being able to access their own long-term abstract phonological representations of the words in the utterance, listeners gain access to a mnemonic standard against which to compare the phonetic idiosyncrasies of an attended talker. Learning the correspondence between an attended talker's consistent phonetics and the listener's long-term representations of phonological categories allows for the construction of a predictive model of that talker's

speech that can be conceptually inverted to help identify that talker. Interestingly, such models of phonetic-phonological correspondence are generative, in that they are able to accurately predict the idiosyncratic properties of a talker's speech even for phonemes that had not been specifically encountered before (Theodore & Miller, 2010). The ability to use models of phonetic-phonological correspondence to help identify talkers depends specifically on linguistic knowledge of the talker's speech. When listening to speech in a foreign language, listeners have no long-term phonological representations of the underlying words against which to compare a talker's phonetics. The specifically linguistic basis for noticing phonetic nuances in talker identification is evinced by studies that demonstrate that the discrepancy between native- and foreign-language voice recognition cannot be overcome without specific linguistic knowledge of the foreign language (Perrachione & Wong, 2007).

1.1.3 The benefits of phonetic variability for speech learning

Phonetic variability also plays an important role in developing phonological representations. Evidence from a number of speech-learning studies indicates that acquiring novel phonological contrasts is facilitated by learning in a high-phonetic-variability training environment (Wang *et al.*, 1999; Flege, 1995; Kingston, 2003; Lively, Logan, & Pisoni, 1993; Clopper & Pisoni, 2004; Barcroft & Sommers, 2005). Listeners who learn from high phonetic variability recognize the novel phonological contrasts more accurately from a wider variety of novel speech sources than those who learn from a more restricted training set. However, there is an important caveat to the utility of high-phonetic variability, such that individuals with weaker perceptual abilities for the target contrasts may actually be disproportionately impaired by the presence of high stimulus variability if they are unable to extract the relevant features to be learned from among the range of between-token variation in irrelevant features (Perrachione *et al.*, 2011).

1.2 Phonological representations and learning to read

Acquisition of reading skill depends on learning to associate arbitrary visual stimuli (in English, letters) with abstract representations of the phonological units of one's language. It is not surprising, then, that an immense literature describes the positive, causal relationship between phonological processing abilities, or metalinguistic phonological awareness, and successful reading development (Bradley & Bryant, 1983; Wagner & Torgesen, 1987; Bryant, *et al.*, 1990), such that young children with greater phonological processing skills tend to be more successful readers early on, and those with weaker skills experience delays in reading acquisition or, in certain cases, profound difficulties in reading development associated with developmental dyslexia. Because the literature associating reading development with phonological processing skills is so extensive, and so adeptly reviewed elsewhere (*e.g.*, Adams, 1994; Pufpaff, 2009; Melby-Lervåg, Lyster, & Hulme, 2012), it will suffice to point out here that different orthographies place different demands on the phonological processing skills of developing readers. In transparent orthographies, where the correspondence between graphemes and phonemes is highly stereotyped and consistent across contexts, the phonological processing load is different than in an orthography like that of English, where a letter may make any of a variety of sounds depending on context or purely arbitrary convention (Ziegler & Goswami, 2005).

1.3 Developmental dyslexia and a phonological deficit

In some instances, individuals experience disproportionate difficulty acquiring reading skills despite sufficient motivation, intelligence, and educational opportunity. In such cases, an individual may have developmental dyslexia:

> "*...a specific learning disability that is neurobiological in origin. It is characterized by difficulties with accurate and/or fluent word recognition and by poor spelling and decoding abilities. These difficulties typically result from a deficit in the phonological component of language that is often unexpected in relation to other cognitive abilities and the provision of effective classroom instruction.*" (Lyon, Shaywitz, & Shaywitz, 2003)

The claim that developmental dyslexia is a neurological condition stems from the fact that it is both significantly familial and heritable (Shaywitz & Shaywitz, 2005). In English, dyslexia is diagnosed based on impairment in single word reading, thus emphasizing decoding over other possible modes of reading impairment, such as difficulties with reading comprehension or reading fluency. However, there has been a recent trend to emphasize a putative "double deficit" in the most seriously impaired readers, in which difficulties with both phonological processing and naming fluency combine to severely undermine typical reading development (Wolf, 1986; Denckla & Rudel, 1976), although this proposition is not without contention (Vaessen, Garretsen, & Blomert, 2009).

Dyslexia has long been understood to be a consequence of underlying disorders of linguistic or perceptual processing that bears on phonological representations, and the current consensus in clinical and research fields considering language and reading development and disorders is that developmental dyslexia predominately results from an impairment in the representation of, or access to, the abstract representations of spoken language (Bradley & Bryant, 1983; Lyon, Shaywitz & Shaywitz, 2003, Vellutino *et al.*, 2004; Ramus & Szenkovits, 2008; Gabrieli, 2009). However, both the specific nature of the phonological impairment and its underlying cause remain unresolved. For instance, compared to their peers, individuals with dyslexia are impaired in phonological awareness tasks such as phoneme elision ("say 'window' without saying '/n/'") and sound blending ("what word do these sounds make? '/m/' '/a/' '/p/'") – deficits which often persist into adulthood (Bruck, 1992). Likewise, individuals with dyslexia often exhibit deficits in phonological working memory, as assessed by nonword repetition, which may carry over into poor verbal working memory generally.

1.3.1 Whither speech perception deficits in dyslexia?

Given the extensive evidence for phonological processing deficits in dyslexia, it is somewhat surprising to note that speech perception deficits are not typically observed in this disorder. There is an extensive literature in which speech perception deficits – or at

least differences – are sought in individuals with versus without dyslexia, but the general consensus from this effort appears to be that dyslexia is not associated with speech perception deficits. Studies that do find differences in speech perception between individuals with and without dyslexia tend to demonstrate only quite moderate effects (Serniclaes *et al.*, 2001; Cheung *et al.*, 2009; Vandermosten *et al.*, 2010), and for every study that finds such an effect, there are numerous others that do not (Hazan *et al.*, 2009; Blomert, Mitterer, & Paffen, 2004; Messaoud-Galusi, Hazan, & Rosen, 2011). In general, reviews of the speech-perception-deficit literature in dyslexia largely come to the conclusion that any speech perception deficits are epiphenomenal to other, known deficits in dyslexia – including attention, phonological working memory, or phonological awareness – and, moreover, have very little statistical relationship to the reading abilities of individuals with dyslexia (Manis *et al.*, 1997; Rosen, 2003). While this conclusion is somewhat curious given the broad consensus as to the existence of phonological deficits in dyslexia, it is worth pointing out that there are likely multiple routes to spoken word recognition that vary in the demands they place on abstract phonological representations (*e.g.*, Grossberg. 1980; Mullennix & Pisoni, 1990; Goldinger, 1998; Goldinger, 2007), and individuals with dyslexia may rely disproportionately on routes that eschew computations of the associations between the speech signal and phonological abstractions (Perrachione *et al.*, 2011).

1.3.2 Non-reading perceptual impairments in dyslexia

In addition to a core phonological deficit and concomitant reading impairment, individuals with dyslexia often exhibit behavioral impairments on low-level perceptual tasks that may involve neither reading nor language. For example, in a frequency-discrimination paradigm, typical readers demonstrate enhanced perceptual thresholds when one of the two tones in each pair is held constant throughout the experiment, whereas no such perceptual enhancement is obtained in individuals with dyslexia (Ahissar *et al.*, 2006). Likewise, a number of studies have shown that the addition of noise is significantly more detrimental to individuals with dyslexia than controls for both auditory and

visual, verbal and non-verbal perceptual tasks (Sperling *et al.*, 2005, 2006; Ziegler *et al.*, 2009; Chait *et al.*, 2007). Perhaps related to difficulty with noise-exclusion, there is some suggestion that individuals with dyslexia may experience disproportionate distraction by competing visual stimuli (Vidyasagar & Pammer, 2009; Moores, Cassim, & Talcott, 2011), although the extent of such reports remains limited. Overall, the range of tasks evincing perceptual deficits in dyslexia appears to be those in which consistent contextual information implicitly guides perceptual performance in typically developing readers (Banai & Ahissar, 2010).

1.3.3 Non-phonological theories of visual deficits in dyslexia

Although reading impairments in dyslexia are currently understood in the context of disordered phonological processing, early investigations frequently ascribed reading impairments to atypicalities in the visual system (hence "word blindness" as an archaic term for this disorder). There nevertheless exist well-developed contemporary theories of dyslexia that assert visual impairments as the principal source of reading impairment. Among these, the most prominent are the magnocellular theory of dyslexia (Stein & Walsh, 1997; which is sometimes also applied to auditory processing: Galaburda, Menard, & Rosen, 1994) and theories positing deficits in mechanisms of visual attention (Vidyasagar & Pammer, 2009).

The notion that dyslexia may involve disordered perceptual or attentional processes in vision is not without evidence. Post-mortem studies of the brains of individuals with dyslexia have revealed putative abnormalities in both the visual and auditory magnocellular pathways (Livingstone *et al.*, 1991, Galaburda, Menard, & Rosen, 1994). Behavioral and brain-imaging studies of visual motion and contrast discrimination have shown differences between individuals with and without reading impairment (Martin & Lovegrove, 1987, Eden *et al.*, 1996); however, like much of the evidence supporting low-level auditory deficits, more nuanced studies of low-level visual differences raise questions about whether these differences may be the spurious result of task designs in

which adaptation or noise-exclusion impairments are the actual source of a group difference (*e.g.,* Sperling *et al.*, 2005, 2006).

Although dyslexia may principally arise due to impaired phonological processing, visual representation and visual attention both play a substantial role in reading and reading development, and, like earlier evidence showing a causal connection between phonological processing and learning to read (Bradley & Bryant, 1983), recent evidence has begun to show the importance of visual attention abilities in successful reading development (Franceschini *et al*., 2012).

1.4 Dysfunctional neural adaptation as a framework for understanding the source of a phonological deficit

In this thesis, I advance the following framework for understanding the source of disordered phonological representations that underlie impaired reading development. First, I suggest that in dyslexia there is an impairment in the ability to learn short-term representations of phonetic consistency in speech stimuli. The inability to form short-term representations of consistency in speech sounds precludes the development of the robust, long-term, abstract phonological categories that encompass those sounds and which are necessary for the phonological awareness abilities involved in sound-to-letter mapping and underlying successful and effective reading development. Second, I suggest that this inability to construct short-term representations of phonetic consistency during speech perception represents a particular, but etiologically critical, instantiation of a generalized, fundamental impairment in learning short-term stimulus consistency in dyslexia. Finally, I suggest that such an impairment in constructing short-term representations of stimulus consistency could plausibly result from a dysfunction of a core neural learning mechanism known in auditory neuroscience as rapid cortical plasticity (Fritz *et al.*, 2003).

The subsequent chapters present evidence to support both the restricted hypothe-

sis (that phonetic consistency learning is impaired in dyslexia) and extended hypothesis (that this is an instantiation of a global learning deficit) that constitute this framework. Chapter 2 addresses the restricted hypothesis that individuals with dyslexia are impaired in their ability to learn short-term representations of phonetic consistency during speech perception, the results of which demonstrate the fundamental nature of impaired phonological representations in dyslexia. Chapter 3 builds the bridge between the restricted hypothesis and the extended hypothesis by demonstrating a neural correlate of impaired learning of short-term phonetic consistency in the dyslexic brain. Chapter 4 presents initial evidence towards the extended hypothesis by revealing that reduced neural sensitivity to stimulus consistency in dyslexia is not limited to speech phonetics, but is evident in the diminished adaptation response to a wide range of auditory and visual, linguistic and non-linguistic stimuli. Specifically, the experiments in each of the following chapters address the following questions in turn: (*1*) Whether individuals with dyslexia exhibit impaired ability to learn to use phonetic consistency in talker identification; (*2*) Whether the brains of individuals with dyslexia show reduced sensitivity to phonetic consistency during speech perception; and (*3*) Whether such exiguous plasticity is specific to speech phonetics, or whether impaired learning of phonetic consistency is just the most etiologically relevant example of a broader dysfunction of general purpose perceptual learning mechanisms.

Are individuals with dyslexia impaired in their ability to learn to use phonetic consistency in talker identification? Recall that the ability to notice consistent individual differences in phonetics contributes to significantly enhanced voice recognition abilities: Listeners recognize voices in their native language more accurately than in a language they cannot understand, and this effect is robust to training without some linguistic knowledge of the foreign language (Perrachione & Wong, 2007). Thus, enhanced recognition of native-language voices presumably results from the ability to compare idiosyncratic properties of talkers' phonetics with listeners' long-term knowledge of the phonological structure of the words those utterances contain. If phonological representa-

tions are indeed impoverished in dyslexia, it may reasonably be expected that the ability of individuals with this disorder to recognize voices will be impaired compared to control listeners with intact phonologies and typical reading ability. Moreover, this effect should be limited to only voices speaking the listeners' native language, as neither individuals with nor without dyslexia would have access to the relevant phonological representations for the foreign language speech. Indeed, this is the result observed in Experiment 1: Individuals with dyslexia are significantly impaired at native-language talker identification compared to controls, but do not differ in their ability to identify foreign language voices. Moreover, the magnitude of voice recognition abilities in dyslexia positively correlates with phonological processing abilities. Together, the experiment and results described in Chapter 2 provide compelling evidence that the ability to learn short-term consistency in speech phonetics is impaired in individuals with dyslexia.

Do the brains of individuals with dyslexia show reduced sensitivity to phonetic consistency during speech perception? We have previously entertained extensive behavioral and neurophysiological evidence that there is a considerable cognitive cost to the perception of speech from multiple, different, unpredictable talkers compared to that from a single, consistent, predictable talker. When attending to speech produced by a single talker, listeners are able to construct a correspondence between the idiosyncratic properties of that individual's speech and their own long-term representations of the sounds of language. This correspondence not only facilitates the speed and accuracy of speech perception, but it is also known to be generative in the sense that it can reliably predict the idiosyncratic properties of even previously unencountered phonemes produced by the attended talker (Theodore & Miller, 2010). Based on functional neuroimaging studies in humans, we further know that such talker adaptation is associated with reduction of the hemodynamic or electrophysiological responses to the speech of the attended talker (Knösche *et al.*, 2002; Belin & Zatorre, 2003; Wong, Nusbaum, & Small, 2004, Kaganovich *et al.*, 2006;), presumably representing an increase in neural efficiency based on predictive coding of the relevant (auditory) perceptual space associated with that in-

dividual talker. If the ability of individuals with dyslexia to learn the phonetic consistencies of individual talkers is impaired, we can reasonably hypothesize that the corresponding neural signature of talker adaptation – namely, reduced hemodynamic response to speech produced by a consistent, predictable talker – will likewise be diminished. That is, we may hypothesize that individuals with dyslexia will show less of a difference in neural response than will controls to speech produced by multiple talkers versus the speech of a single talker. Indeed, this is the result observed in Experiment 2: The magnitude of neural adaptation to a consistent talker is significantly diminished in dyslexia, reflecting a reduced sensitivity of auditory cortex to short-term phonetic consistency.

Is exiguous plasticity specific to perceiving consistency in speech phonetics, or is it evident in the encoding of stimulus consistency across perceptual domains? Finally, we have reviewed a number of non-reading deficits exhibited by individuals with dyslexia that lead to the supposition that impaired learning of short-term phonetic consistency (and, correspondingly, the reduced neural adaptation to this consistency) may be a salient instantiation of dysfunction in a domain-general perceptual learning mechanism supported by rapid cortical plasticity. If this is the case, we would expect to see similarly reduced neural adaptation to predictable stimulus consistency in other domains. This hypothesis is addressed in Experiment 3, in which diminished neural adaptation is observed in individuals with dyslexia to auditory and visual, linguistic and non-linguistic stimuli: spoken and written words, visual objects, and faces.

This collection of results provides substantial evidence for impaired learning of phonetic consistency as a core deficit in dyslexia, which is a strong candidate for the source of impoverished phonological representations that underlie disordered reading development. Moreover, the results of Experiment 3 provide compelling initial evidence that such a disorder is not specific to either auditory or linguistic processing, but may represent a fundamental dysfunction in the mechanisms of rapid cortical plasticity that

allow for adaptation to stimulus consistency and which support the development of robust representations of perceptual categories. Chapter 5 considers how this framework for understanding the source of impaired phonological representations is supported by an extensive literature on rapid plasticity in animal models of perceptual learning, as well as is consistent with the existing literature on the neural bases of dyslexia. Finally, Chapter 5 also describes questions that data from the present experiments are insufficient to answer, as well as makes more specific predictions as to which biological processes are reasonable targets for future research into understanding the mechanistic basis of diminished neural adaptation (and underlying rapid plasticity dysfunction) in dyslexia.

2. Phonologically-based voice recognition deficits in dyslexia[1]

The ability to recognize people by their voice is an important social behavior. Individuals differ in the phonetic properties of their speech productions, and listeners may take advantage of their language-specific knowledge of speech phonology to perceive these differences and facilitate recognizing voices. Impaired phonological processing is characteristic of dyslexia and thought to be a basis for difficulty learning to read. We tested the voice-recognition abilities of dyslexic and control listeners for voices speaking either listeners' native language or an unfamiliar, foreign language. Individuals with dyslexia exhibited impaired voice-recognition abilities compared to controls only for voices speaking their native language. These results demonstrate the fundamental disruption of phonological representations in dyslexia and the importance of linguistic representations for voice recognition. Humans appear to identify voices by making comparisons between talkers' idiosyncratic pronunciations of words and listeners' stored abstract representations of the sounds in those words.

2.1 Introduction

The ability to recognize individual conspecifics is an adaptive trait evinced broadly among social and territorial animals, including species as diverse as horses (Proops, McComb, & Reby, 2009), penguins (Jouventin, Aubin, Lengagne, 1999), fish

[1] *Portions of this chapter were originally published as T.K. Perrachione, S.N. Del Tufo, and J.D.E. Gabrieli (2011). "Human voice recognition depends on language ability."* Science*, 333, 595.*

(Grosenick, Clement, & Fernald, 2007), and lobsters (Karavanich & Atema, 1998). Recognition of individuals from their communicative vocalizations is common across species (Insley, 2000; Janik, Sayigh, & Wells, 2006; Kazial, Kenny, & Burnett, 2008; Proops, McComb, & Reby, 2009), including humans.

The combination of discrete articulatory units (phonemes) through rule-governed constraints (phonology) makes human speech one of the most complex and prolific forms of vocal communication in the animal kingdom. Although the human vocal tract can produce a wide variety of speech sounds, languages differ in the number and types of these sounds used. During language acquisition, children become experts in perceiving the speech sounds used in their native language, while simultaneously losing the ability to distinguish foreign language speech sounds (Werker & Tees, 1984; Polka *et al.*, 2001; Kuhl, 2004; Werker & Tees, 2005). Because of this extensive expertise with the speech sounds of their native language, listeners exhibit a "language-proficiency effect" in talker identification, in which they are more accurate at identifying voices speaking a language they understand than one they do not (Thompson, 1987; Goggin *et al.*, 1991). This effect has been shown to depend specifically on linguistic processing, cannot be overcome without some competence in the foreign language (Perrachione & Wong, 2007), and likely involves neural processes that integrate the talker-specific idiosyncrasies of perceived speech with long-term abstract internal representations of speech sounds (Knösche *et al.*, 2002; Kaganovich *et al.*, 2006; Wong, Nusbaum, & Small, 2004; Perrachione, Pierrehumbert, & Wong, 2009; Chandrasekaran, Chan, & Wong, 2011; Sjerps, Mitterer, & McQueen, 2011). Specifically, by being able to compute the difference between the phonetics of an individual talker's productions and listeners' long-term abstract (phonological) representations of the speech sounds comprising an utterance, listeners gain access to a highly expository source of information about talker identity above and beyond what is available in language-independent voice-structure cues (Belin, Fecteau, & Bédard, 2004; Winters, Levi, & Pisoni, 2008; Levi, Winters, & Pisoni, 2011).

Being able to compute the differences in phonetics across individuals necessarily

requires specific, robust, abstract representations of the underlying speech sounds against which to compare any novel speech sample. Some speakers of a language may nevertheless be unable to bring such robust phonological representations to bear for talker-identification tasks. In particular, individuals with dyslexia are known to perform poorly on measures of phonological processing compared to their peers (Snowling, Wagtendonk, & Stafford 1988; Shankweiler *et al.*, 1995). Indeed, reading difficulties in languages like English are most frequently attributed to underlying deficits in phonological processing – the representation of speech sounds and knowledge of how they can be manipulated (Bradley & Bryant, 1983; Wagner & Torgesen, 1987). However, there remains some debate about the specific nature of the phonological processing deficit in dyslexia: Are the phonological representations themselves impoverished, or do phonological processing difficulties associated with reading impairment involve a deficit in higher-level phonological awareness – the conscious, metalinguistic access to the sounds of language and how they can be manipulated (*e.g.*, Ramus & Szenkovits, 2008)?

In the present experiment, we examine the abilities of English-speaking individuals with and without dyslexia for learning to recognize voices that speak either the listeners' native language (English) or an unfamiliar, foreign language (Mandarin Chinese). In such a task, control participants with normal reading development and phonological abilities are expected to be more accurate at voice recognition in their native language than the foreign one, as demonstrated previously (Goggin *et al.*, 1991; Perrachione & Wong, 2007; Perrachione, Pierrehumbert, & Wong, 2009). Theories postulating different underlying disorders in dyslexia make different predictions about the patterns of voice recognition abilities these individuals will display. If dyslexia results from a core auditory processing deficit (Tallal & Piercy, 1973; Nagarajan *et al.*, 1999; Ahissar *et al.*, 2000; Goswami, 2011), individuals with this disorder would most likely have global deficits in voice recognition learning, due to the demanding auditory perceptual requirements of this task. Alternately, if reading impairment in dyslexia results from deficits in phonological awareness (Ramus & Szenkovits, 2008), individuals with this dis-

order should display a pattern of voice recognition abilities consistent with unimpaired control listeners, since explicit, metalinguistic phonological processing is not required in voice recognition. Finally, if dyslexia is characterized by fundamentally impoverished phonological representations themselves, then, compared to controls, individuals with this disorder should demonstrate impaired native-language voice recognition, which is facilitated by implicit phonological processing, but unimpaired foreign-language voice recognition, which does not depend on phonological processing.

2.2 Methods

2.2.1 Participants

Native English-speaking controls (N = 16; 9 female) 18-30 years of age (M = 21.2; SD = 2.98) with a self-reported history free from neurological, psychiatric, speech, language, or reading impairments were matched with individuals with dyslexia (N = 16; 8 female) between 16-38 years of age (M = 24; SD = 6.8). Inclusionary criteria for dyslexia consisted of a prior clinical diagnosis or lifelong history of reading disability and scoring below the 16th percentile (one standard deviation below the age-normed mean) on any two subtests from the following standard clinical reading and language assessments: *Woodcock Reading Mastery Test-Revised* (WRMT-R/NU) (Woodcock, 1998), *Test of Word Reading Efficiency* (TOWRE) (Torgesen, Wagner, & Rashotte, 1999), and *Comprehensive Test of Phonological Processing* (CTOPP) (Wagner, Torgesen, & Rashotte, 1999). Groups did not differ on cognitive performance ("Matrices" and "Block Design" from the *Wechsler Abbreviated Scale of Intelligence*, WASI; (Wechsler, 2008)), working memory (*Wechsler Adult Intelligence Scale,* WAIS-IV; (Wechsler, 1999)), age, or education (Table 2.1). All participants indicated no prior experience with Mandarin Chinese. Informed written consent, approved by the MIT Committee on the Use of Humans as Experimental Subjects, was obtained from all participants prior to participation.

		Control		Dyslexia		
Test	Subtest	Raw Score	Standard Score	Raw Score	Standard Score	Cohen's *d*
WASI						
	Block Design	60.6 ± 7.4	61.4 ± 5.4	53.9 ± 13.4	57.1 ± 8.1	0.644
	Matrix Reasoning	29.8 ± 2.3	58.6 ± 4.7	29.8 ± 3.8	58.4 ± 6.8	0.022
	Performance IQ	119.9 ± 8.5	116.8 ± 8.8	115.5 ± 11.0	112.2 ± 11.0	0.487
CTOPP						
	Elision	18.9 ± 1.5	10.9 ± 1.5	15.7 ± 3.4	8.3 ± 2.3	1.401
	Blending Words	18.5 ± 1.4	12.5 ± 1.4	14.1 ± 3.5	8.9 ± 2.5	1.833
	Non-word Repetition	15.7 ± 2.1	11.8 ± 1.9	9.7 ± 1.9	6.8 ± 1.3	3.134
	Rapid Digit Naming	22.9 ± 5.1	10.4 ± 2.6	31.2 ± 8.6	6.9 ± 2.8	1.315
	Rapid Letter Naming	22.8 ± 4.5	11.1 ± 2.7	35.4 ± 8.9	5.5 ± 2.9	2.072
	Rapid Object Naming	39.4 ± 5.6	10.6 ± 3.1	51.7 ± 8.5	6.3 ± 2.1	1.721
WRMT-R/NU						
◊	Word ID	101.7 ± 2.8	112.4 ± 8.1	91.3 ± 6.9	94.2 ± 7.8	2.368
◊	Word Attack	42.4 ± 1.7	121.3 ± 13.3	31.6 ± 4.4	92.0 ± 8.0	2.762
TOWRE						
◊	Sight Word Reading	99.0 ± 8.3	106.1 ± 11.3	79.9 ± 15.4	85.3 ± 13.0	1.765
◊	Decoding	54.7 ± 6.1	104.8 ± 11.4	35.4 ± 10.7	76.7 ± 18.3	1.899
	Total	200.0 ± 40.9	106.5 ± 11.6	166.2 ± 21.9	75.4 ± 19.8	1.975
WAIS-IV						
	Digit Span Total	8.6 ± 1.5	9.6 ± 1.9	7.9 ± 1.9	8.8 ± 2.5	0.403
Age (years)		21.3 ± 2.7		23.9 ± 6.8		0.536
Education (years)		15.3 ± 1.5		15.1 ± 2.4		0.286

Table 2.1: Cognitive, behavioral, and demographic assessment of participants in Experiment 1. Values are mean ± standard deviation. Cohen's *d* shows the effect size of the group difference in standard scores. Diamonds (◊) denote tests used as inclusionary/exclusionary criteria for group membership. Abbreviations: WASI: *Wechsler Abbreviated Scale of Intelligence*, 3rd Ed.; CTOPP: *Comprehensive Test of Phonological Processing*; WRMT-R/NU: *Woodcock Reading Mastery Test-Revised*, TOWRE: *Test of Word Reading Efficiency*; WAIS-IV: *Wechsler Adult Intelligence Scale*.

2.2.2 Stimuli

Two sets of ten sentences designed for acoustic assessment were recorded for this experiment: one spoken in English (IEEE, 1969), the other in Mandarin (Open Speech Repository, 2005). The English sentences were read by five male native speakers of American English (aged 19-26 years, M = 21.6). The Mandarin sentences were read by five male native speakers of Mandarin Chinese (aged 21-26 years, M = 22.6). No talker read sentences in both languages, and none of the individuals recorded as talkers partici-

pated in the listening experiment. Recordings were made in a sound-attenuated chamber via a SHURE SM58 microphone using a Creative USB Sound Blaster Audigy 2 NX sound card, sampled at 22.05 kHz and normalized for RMS amplitude to 70 dB SPL. Recordings of sentences were 1.46s to 4.09s in duration (M = 2.43, SD = 0.54). In each language, five sentences were used during the familiarization and practice phases, and all ten were used during the final voice recognition test. These stimuli have been used in prior experiments of voice recognition by native speakers of English and Chinese (Perrachione & Wong, 2007; Perrachione, Pierrehumbert, & Wong, 2009).

2.2.3 Procedure

Participants learned to identify five talkers in each of two language conditions (English and Mandarin) from the sound of their voice. Each talker was associated with a distinct cartoon avatar (Fig. 2.1). Training and testing on voice recognition were completed in each language condition separately, and the order was counterbalanced across listeners. During an initial familiarization phase, participants heard each of the voices in succession while the corresponding avatars were displayed on a computer screen. Participants then actively practiced identifying the talkers with corrective feedback: The five avatars appeared on the screen while a recording from one talker was played, and participants selected the avatar matching the voice they heard. If participants selected incorrectly, the computer indicated the correct response. During the task, all instructions were presented both as text on the screen and as auditory prompts recorded by an additional female talker. The familiarization and active practice phases were repeated over five training sentences, and each sentence was practiced ten times. Following training, participants undertook a 50-item talker identification test, in which they identified the voices without feedback. Participants completed the self-paced experiment in a quiet room. Stimuli were presented binaurally at a comfortable level over Sennheiser HD-250 linear II circumaural headphones using an Edirol UA-25EX sound card.

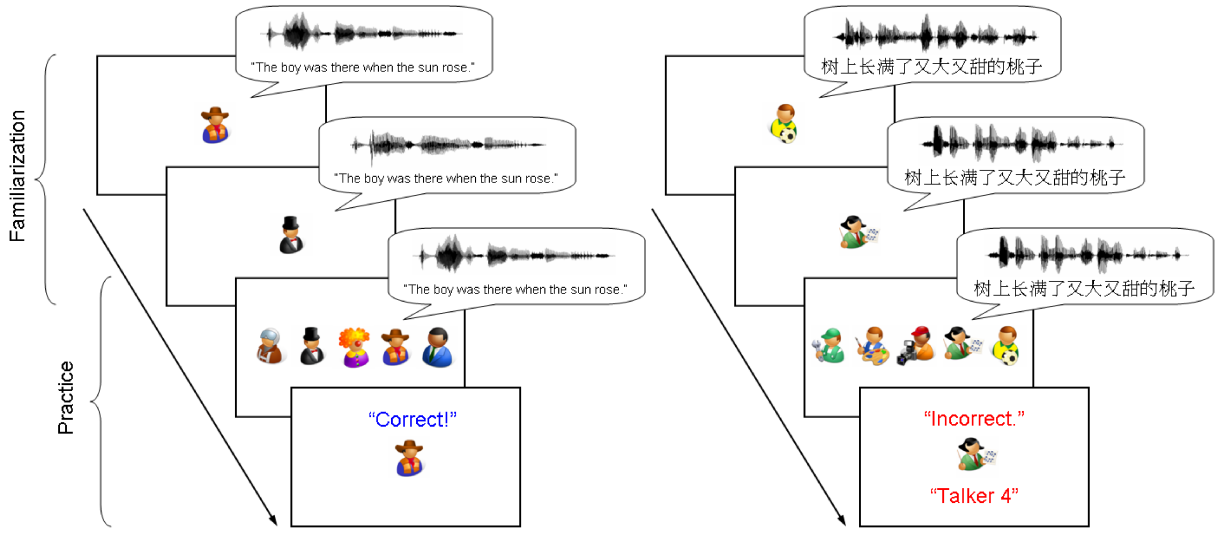

Figure 2.1: Graphical depiction of training paradigm. Listeners learned to recognize 5 English and 5 Chinese talkers from the sound of their voice. Talkers were paired with distinct icons, and acoustic waveforms illustrate variability in talker characteristics. Participants were familiarized with individual talkers and practiced recognizing them with feedback. Talker identification accuracy in each condition was assessed with a post-training test.

2.3 Results

All statistical analyses were conducted in R[2] v2.14.1. Participants' accuracy on the voice recognition tests was analyzed with a 2×2 analysis of variance of a linear mixed effects model, with Condition (English vs. Mandarin; within-subjects) and Group (control vs. dyslexia; between-subjects) as random factors and participants as a fixed factor (Fig. 2.2). Dyslexic participants exhibited significantly impaired voice recognition abilities compared to controls in the native language condition, but not the foreign-language condition [Group × Condition interaction; $F(1,30) = 14.82$, $p < 0.0006$]. Because of the enhanced performance of control participants in their native language, there was better overall voice-recognition accuracy in that condition [main effect of Condition; $F(1,30) =$

[2] *R: http://www.r-project.org/*

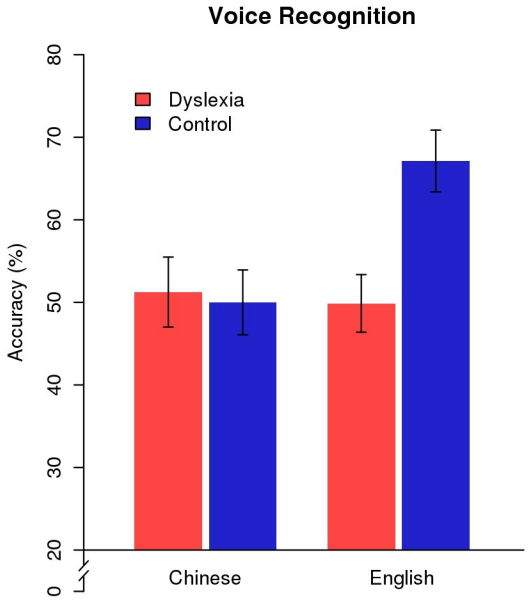

Figure 2.2: Mean voice recognition performance of dyslexic and control listeners (error bars: standard error of the mean). All individuals scored above chance (20%), shown as baseline.

10.74, $p < 0.003$], as well as a trend towards overall more accurate voice recognition by the control group [main effect of Group; $F(1,30) = 2.67$, $p = 0.113$]. We confirmed this interpretation through a series of planned comparisons (all t-tests are two-tailed, and paired- or independent-sample as appropriate). The control group exhibited more accurate voice recognition in their native language than the foreign one [$t(15) = 4.52$, $p < 0.0005$, Cohen's $d = 1.15$]. Controls were also more accurate at native-language voice recognition than the dyslexic participants [$t(30) = 3.37$, $p < 0.0021$, $d = 1.23$], demonstrating dyslexics' impaired ability to take advantage of the phonological cues that enhance controls' native-language talker identification. Correspondingly, dyslexic participants' accuracy did not differ between the two language conditions [$t(15) = 0.47$, $p = 0.65$.], suggesting they employ similar (*i.e.*, non-phonological) voice-recognition strategies regardless of whether the attended utterances were comprehensible. The two groups did not differ in their accuracy for foreign-language voices [$t(30) = 0.22$, $p = 0.83$], demonstrating dyslexia had no effect on the basic auditory abilities used for voice recognition when phonological information is unavailable. All participants performed above

chance (20%) in both conditions. In sum, these results demonstrate a profound impairment in voice recognition among listeners with dyslexia for native- but not foreign-language speaking talkers.

Because maximally successful native-language voice recognition is thought to depend largely on recognizing talker-specific phonetic idiosyncrasies (*i.e.*, how each talker's pronunciations are different and distinctive), we investigated the relationship between participants' cognitive capacity for processing speech sounds (as measured by standardized clinical assessments of phonological processing; Wagner, Torgesen, & Rashotte, 1999) and their performance on the voice recognition task in the two languages (Fig. 2.3). Standard clinical measures of dyslexic participants' phonological processing ability correlated positively and significantly with their ability to recognize English-speaking voices [phonological memory: $r = 0.60$, $p < 0.015$; phonological awareness: $r = 0.61$, $p < 0.012$], but not Mandarin-speaking ones [both $r > 0.33$, *n.s.*]. That is, listeners with dyslexia exhibiting the greatest impairment in phonological processing also exhibited the least accurate native-language voice recognition and *vice-versa*. This relationship was not seen in control participants.

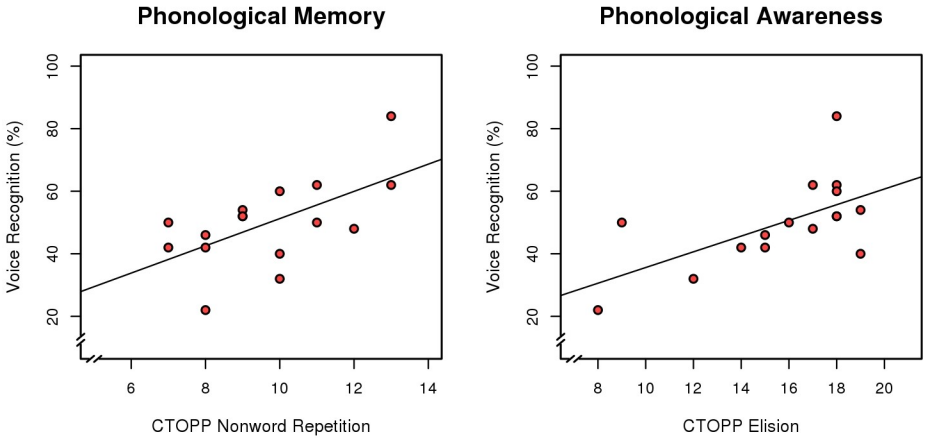

Figure 2.3: Relationships between voice recognition ability in dyslexia and clinical measures of phonological working memory (nonword repetition) and phonological awareness (phoneme elision) from the CTOPP, *Comprehensive Test of Phonological Processing,* (Wagner, Torgesen, & Rashotte, 1999).

2.4 Discussion

This experiment examined voice recognition ability in English-speaking individuals with and without dyslexia. Compared to control participants with normal reading development, participants with dyslexia demonstrated significantly reduced ability for recognizing voices in a known language (English), but did not differ in the ability to recognize voices in an unknown foreign language (Mandarin). Only the control group showed canonically superior performance for their native language. Familiar-language voice-recognition performance by individuals with dyslexia was significantly related to their phonological processing abilities, such that individuals scoring higher on measures of phonological processing also were more accurate at voice recognition. This relationship was not observed in the foreign language condition.

By showing a phonologically-based voice-recognition deficit in dyslexia, these results clarify the nature of the phonological processing deficit in this disorder in three important ways. First, the fact that individuals with dyslexia exhibit impaired voice recognition abilities only in their native language and not a foreign one is inconsistent with the idea of a general, low-level auditory processing deficit in dyslexia (Ahissar *et al.*, 2000; Goswami, 2011). If dyslexia was characterized by a core deficit in auditory processing, deficits in voice recognition would have been expected independent of linguistic content. Second, these results suggest that deficits in phonological processing are not specific either to metalinguistic tasks (*e.g.*, conscious access to phonology, as in rhyming) or to tasks that require rapid naming (Ramus & Szenkovits, 2008). Instead, the phonological processing deficit significantly affects the ecological, self-paced, and putatively non-linguistic task of voice recognition. Third, a deficit in phonological processing is not somehow specific to integrating phonological information across sensory modalities, as is necessary during mapping between speech sounds and written text (Blau *et al.*, 2009), as we observed the effects of impairments in phonological processing during a strictly auditory task.

It is worth distinguishing the voice-recognition impairment observed in dyslexia from classical agnosias and other deficits in social perception. There exist other disorders in which the ability to recognize individuals is impaired, including prosopagnosia for faces (Hecaen & Angelergues, 1962) and phonagnosia for voices (Van Lancker & Canter, 1982; Van Lancker & Kreiman, 1987; Hailstone *et al.*, 2010), but these are typically either associated with specific neurological insult or are part of global deficits in object recognition. The deficit in voice recognition evinced by individuals with dyslexia does not represent a general deficit in recognition abilities, as these individuals do not demonstrate abnormal face perception (Brachacki, Fawcett, & Nicolson, 1994; Rüsseler, Johannes, & Munte, 2003; Smith-Spark & Moore, 2009), visual object recognition (Snowling, 1998), or impaired recognition of foreign-language voices. Instead, impaired voice-recognition abilities in dyslexia further demonstrate fundamentally impoverished phonological representations in this disorder, as well as the critical role of linguistic processing in human voice recognition.

Principally, these results demonstrate that there is a fundamental impairment of phonological processing in dyslexia such that individuals with this disorder are insensitive to the phonetic idiosyncrasies that exist between talkers; the ability to encode such information necessarily requires abstract phonological representations against which to compare the phonetic variation among talkers. This stands in contrast to the idea that individuals with dyslexia have a more selective disorder of phonological awareness (the metalinguistic access to phonological representations critically important for typical reading development) alone (Ramus & Szenkovits, 2008). Correspondingly, these results also bear on our understanding other behavioral and perceptual deficits observed in dyslexia. In addition to explicitly identifying individuals, voice recognition abilities allow listeners to keep track of who said what in conversations involving multiple talkers, as well as attend to a single talker when many people are speaking simultaneously, such as at the proverbial cocktail party. A deficit in voice recognition renders both of these tasks substantially more difficult, and may thus explain dyslexics' difficulties in tasks that re-

quire robust representation of the nuances of individual talkers' phonetics, including, the perception of speech in noise (Ziegler *et al.*, 2009, Chandrasekaran *et al.*, 2009) and categorical perception (Serniclaes *et al.*, 2004).

That individuals with a deficit in phonological processing exhibit a concomitant deficit in voice recognition further reveals the unique importance of humans' linguistic capacity in our social auditory behavior. Most of our experience identifying individuals from their vocalizations involves listening to comprehensible speech, and, as such, listeners learn talkers' identity not only from the distinctive structural features of their vocal apparatus, but also from the unique ways talkers manipulate their vocalizations to convey linguistic content. By obfuscating the link between talkers' idiosyncratic phonetics and the abstract phonological categories they comprise – either in the stimulus, as in foreign-language speech, or in its mental representation, as in dyslexia – listeners' ability to recognize individuals by voice is severely impaired. Although other animals use variability in communicative vocalizations to identify individual conspecifics (*e.g.*, Lengagne *et al.*, 2000; Janik, Sayigh, & Wells, 2006), the complex, dynamic, and culturally-specific features human listeners use to identify one another demonstrate the importance of our language capacity in shaping auditory expertise.

3. Reduced neural sensitivity in dyslexia to phonetic consistency in speech perception

Talker adaptation occurs rapidly during speech perception when listeners learn the correspondence between their long-term abstract representations of speech sounds and the idiosyncratic phonetic properties of an attended talker. Constructing this correspondence facilitates both the speed and accuracy of speech perception by reducing the cognitive, and therefore physiological, demands on the auditory perceptual system. The neurophysiological correlates of talker adaptation are evident in reduced electrophysiological or hemodynamic response to the speech of a single consistent talker versus multiple unpredictable ones. To further understand the nature of impaired phonological processing in dyslexia, in this experiment we used fMRI adaptation to measure differences between individuals with and without dyslexia in neural adaptation to phonetic consistency during a speech perception task.

3.1 Introduction

One prominent ecological source of rapid perceptual adaptation in human behavior is the phenomenon of "talker adaptation" (sometimes called "talker normalization") in speech perception. Listeners are faster and more accurate at understanding spoken language when they have adapted to an individual talker's voice (Nygaard, Sommers, & Pisoni, 1994), and the specificity of adaptation to talkers' idiosyncratic phonetic features

guides the perception of spoken words (Theodore & Miller, 2010). Functional neuroimaging experiments of speech perception have shown that listening to speech from a consistent talker results in reduced activation in auditory sensory and association cortices (Belin & Zatorre, 2003; Wong, Nusbaum, & Small, 2004; Chandrasekaran, Chan, & Wong, 2011), suggesting that rapid cortical plasticity underlies the behavioral benefits of talker adaptation. Individuals with dyslexia, however, do not utilize differences in spoken language phonetics between talkers to enhance perception (Perrachione, Del Tufo, & Gabrieli, 2011), perhaps because they are unable to learn the perceptual correspondence between talkers' idiosyncratic phonetics and long-term abstract phonological representations.

We therefore hypothesized that the magnitude of neural adaptation to the consistent phonetics of a repeated talker would be reduced in individuals with dyslexia compared to typically-reading controls. In Experiment 2, we used fMRI to compare activation between individuals with dyslexia and typically-reading control participants while they performed an auditory-word to visual-picture matching task. Auditory words were spoken either by a single, consistent talker ("Adaptation" condition) or by four different, inconsistent talkers ("No-Adaptation" condition). In the Adaptation condition, the trial-by-trial consistency in the talker's voice and phonetics should result in reduced activation in cortical areas supporting speech perception as listeners adapt to the single talker’s speech across different words.

3.2 Methods

3.2.1 Participants

Two groups of adult participants were recruited for this study: (*1*) individuals with a prior dyslexia diagnosis or lifelong history of reading difficulties (N = 19), and (*2*) controls (N = 19), who had a self-reported history free from reading difficulty. All subjects were native speakers of American English and had a self-reported history free

from additional language, speech, or peripheral hearing disorders, and reported no other known psychological or neurological disorders.

To confirm participants' status as typical or impaired readers, their performance on a battery of standardized intelligence, memory, reading, and phonological measures was assessed. Performance at or below the 25th percentile on two or more subtests of timed or untimed word or nonword reading comprised inclusionary criteria for the dyslexia group. Performance at or below the 25th percentile on any one such subtest comprised exclusionary criteria from the control group. All participants scored at or above average on measures of performance IQ and working memory. Enumeration of the specific assessments used, as well as group average performance on these measures and basic demographics, are reported in Table 3.1.

3.2.2 Stimuli

Audio stimuli consisted of 288 monosyllabic nouns read in isolation by five adult female native English-speakers, which were recorded in a sound-attenuated chamber via a SHURE SM58 microphone. Stimuli were sampled at 44.1 kHz using an Edirol UA-25EX sound card, and normalized for RMS amplitude to 70 dB SPL using Praat[1] (Boersma, 2001). Normalized stimuli were spectrally filtered to attain frequency response equalization for binaural presentation via a pair of Sensimetrics (Malden, MA) S-14 MRI-compatible insert earphones. Recordings of words were 204ms to 1180ms in duration (M = 531, SD = 149). Of the 288 words, 36 were selected as targets, for which corresponding images were selected from a standard set (Snodgrass & Vanderwart, 1980). Images consisted of black line figures against white backgrounds, 300×300 pixels at 72dpi.

3.2.3 Procedure

Participants lay supine in an MRI scanner and undertook a auditory-word to visual-picture matching task during sparse-sampling fMRI. In the task, participants saw

[1] *Praat: http://www.fon.hum.uva.nl/praat/*

target images presented on the projection screen while listening to the isolated auditory word stimuli (Fig. 3.1). Participants' task was to press a button indicating when the word they heard matched the picture they saw. This task was performed alternately under two conditions: (*1*) an "Adaptation" condition, in which the auditory stimuli were produced

		Control		Dyslexia		
Test	Subtest	Raw Score	Standard Score	Raw Score	Standard Score	Cohen's *d*
WASI						
	Block Design	62.1 ± 5.9	62.4 ± 4.0	52.3 ± 14.0	56.4 ± 9.2	0.860
	Matrix Reasoning	30.9 ± 1.7	60.7 ± 3.4	29.3 ± 3.3	58.1 ± 7.3	0.453
	Performance IQ	123.1 ± 5.5	119.7 ± 5.6	114.5 ± 13.8	112.4 ± 12.6	0.766
CTOPP						
	Elision	19.5 ± 0.7	11.5 ± 0.7	16.1 ± 2.8	8.5 ± 1.9	2.061
	Blending Words	18.0 ± 1.1	12.0 ± 1.1	14.6 ± 4.1	9.5 ± 3.0	1.091
	Non-word Repetition	15.3 ± 1.6	11.7 ± 2.7	10.0 ± 1.6	6.9 ± 1.0	2.456
RAN						
	Numbers	15.7 ± 1.6	113.7 ± 3.3	23.4 ± 5.3	103.1 ± 7.4	1.887
	Letters	15.7 ± 1.6	113.7 ± 3.3	23.4 ± 5.3	103.1 ± 7.4	1.887
	Numbers & Letters	15.7 ± 1.7	112.1 ± 3.0	23.6 ± 6.3	99.9 ± 9.3	1.781
WRMT-R/NU						
	◊ Word ID	101.4 ± 3.6	113.0 ± 11.5	89.7 ± 7.5	91.1 ± 10.5	2.064
	◊ Word Attack	40.7 ± 2.6	112.9 ± 12.5	31.8 ± 3.6	91.6 ± 6.9	2.217
	Passage Comprehension	17.0 ± 1.6	116.4 ± 4.2	27.8 ± 8.7	99.7 ± 10.5	2.134
TOWRE						
	◊ Sight Word Reading	100.5 ± 4.7	107.1 ± 7.9	80.0 ± 9.0	83.4 ± 7.1	3.288
	◊ Decoding	56.7 ± 5.7	108.5 ± 10.5	34.8 ± 10.4	79.2 ± 9.4	3.040
	Total	204.0 ± 40.5	109.3 ± 7.2	162.6 ± 15.2	77.5 ± 9.0	4.003
WJ-III						
	Fluency	103.6 ± 19.1	120.9 ± 13.2	64.7 ± 15.3	94.0 ± 10.8	2.318
WAIS-IV						
	Digit Span Total	34.4 ± 6.0	13.4 ± 3.3	25.8 ± 4.7	8.6 ± 2.3	1.733
Age (years)		22.1 ± 3.7		24.5 ± 5.9		0.494
Education (years)		15.3 ± 1.6		14.9 ± 2.3		0.184
Sex		9 M / 10 F		7 M / 12 F		0.053 (φ)

Table 3.1: Cognitive, behavioral, and demographic assessment of participants in Experiment 2. Values are mean ± standard deviation. Cohen's *d* shows the effect size of the group difference in standard scores. Diamonds (◊) denote tests used as inclusionary/exclusionary criteria for group membership. Abbreviations: WASI: *Wechsler Abbreviated Scale of Intelligence*, 3rd Ed. (Wechsler, 2008); CTOPP: *Comprehensive Test of Phonological Processing* (Wagner, Torgesen, & Rashotte, 1999); WRMT-R/NU: *Woodcock Reading Mastery Test-Revised* (Woodcock, 1998); TOWRE: *Test of Word Reading Efficiency* (Torgesen, Wagner, & Rashotte, 1999); WAIS-IV: *Wechsler Adult Intelligence Scale* (Wechsler, 1999).

by a single, consistent talker; and (*2*) a "No-Adaptation" condition, in which the auditory stimuli were produced by four different, unpredictable talkers. Participants underwent four runs of this task, each of which consisted of nine blocks of each condition, as well as nine blocks of rest. The order of the conditions and rest blocks was pseudorandomized using a block-randomization procedure with the constraint that the same condition or rest did not occur in two immediately sequential blocks. Each task block (22s, four TRs) consisted of 2 target images shown in succession for 11s each. Each target image was accompanied by 8 binaural auditory word stimuli (750ms ISI, four words per TR delay), one of which matched the visual image and to which the participant pushed the button. No audio stimuli were played during image acquisition, but the target image remained on the screen. There was a 500ms delay between the end of the acoustic noise resultant from scanner acquisition and the onset of auditory stimulation. Rest blocks were also 22s (four TRs), during which participants maintained fixation on a white "+" symbol in the

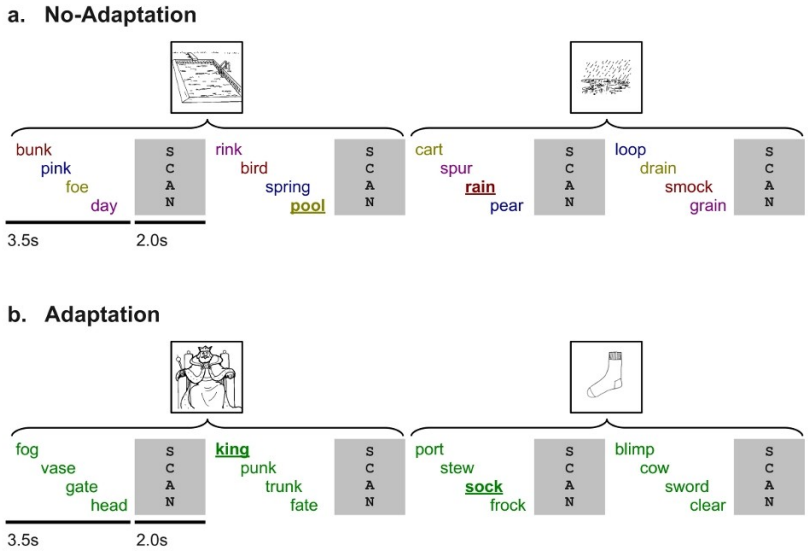

Figure 3.1: Design of stimulation paradigms in Experiment 2. **(a)** Neural adaptation to consistency in phonetics of speech stimuli was measured during a speech perception task. A picture was shown on the projection screen while participants heard a sequence of auditory words. Participants indicated when the auditory word matched the picture (indicated here in bold, underlining). Sparse sampling was used so auditory stimuli could be presented without contamination by scanner acoustic noise; timing and duration of MR-volume acquisitions are indicated by "scan". Colored text indicates speech from multiple vocal talkers, or **(b)** a single, consistent talker.

center of the screen. The projector background remained at 31.25% luminance throughout the experiment. Across the four runs, the audio words and visual pictures occurred equally in the Adaptation and No-Adaptation conditions, and each of the No-Adaptation talkers was equally likely to produce any target word. Of the five voices, the one used in the Adaptation condition (and the corresponding four in the No-Adaptation condition) was permuted across participants.

3.2.4 MRI Data Acquisition

Data were acquired on a Siemens Trio 3T scanner with a 32-channel phased array head coil. A whole-head, high-resolution T1-weighted multi-echo MPRAGE anatomical volume (acquisition parameters: TR = 2350ms, TE = {1.79ms, 3.71ms, 5.63ms, 7.55ms}, TI = 1400ms, flip angle = 7°, FOV = 256 × 256, 176 slices, voxel resolution = 1.0 × 1.0 × 1.0mm) was acquired at the beginning of each session.

Four functional runs containing 110 volumes each were collected using sparse-sampled T2*-weighted EPI scans (acquisition parameters: TR = 5500ms, TA (acquisition time) = 2000ms, TE = 30ms, flip angle = 90°, voxel resolution = 3.125 × 3.125 × 4.0mm, FOV = 64 × 64, 32 transverse slices providing whole-brain coverage). Each run was preceded by the four additional TRs from which no data were recorded to allow for stabilization of longitudinal magnetization. Sparse-sampling (Hall *et al.*, 1999; Belin, *et al.*, 1999) was used to allow auditory stimuli to be presented in silence, both to avoid compression of BOLD signal dynamic range in auditory cortex due to acoustic noise in the MR environment (Gaab, Gabrieli, & Glover, 2007), as well as to avoid noise-related hearing difficulties, which often accompany dyslexia (Ziegler *et al.*, 2009).

3.2.5 MRI Data Analysis

Cortical reconstruction and parcellation of anatomical images was performed using the default processing stream in Freesurfer[2] v5.0.0 (Dale *et al.*, 1999). Functional

[2] *FreeSurfer: http://surfer.nmr.mgh.harvard.edu/*

data were analyzed in SPM8[3] using workflows in Nipype[4] v0.4 (Grogolewski *et al.*, 2011). Image preprocessing consisted of motion correction (rigid-body realignment to the mean EPI image from the first functional run) and spatial smoothing (6mm isotropic FWHM 3D Gaussian kernel). Motion and intensity outliers (functional volumes exceeding 1mm in differential motion or differing from the mean image intensity by > 3 SD) were identified using ART[5] and regressed out of the hypothesized timeseries. The number of regressed outliers did not differ between the two groups [$F(1,36) = 1.73$, $p = 0.20$]. Model design was implemented using the modelgen algorithm in Nipype, and included two task regressors (for the No-Adaptation and Adaptation conditions, respectively), six motion parameters, individual regressors for any outlier volumes, five Legendre polynomial terms to account for low-frequency components of the MR-signal including scanner drift, and a constant term. Within-subject estimation of the general linear model and contrasts were conducted in participants' native EPI space.

To account for the discontinuous nature of the measured fMRI timeseries as a result of sparse-sampling, additional steps were taken to optimize the hypothesized response timeseries comprising the task regressors (Fig 3.2). For each task condition, a high temporal-resolution vector was created of the onsets of all events as unit impulse responses, where the presentation of four auditory stimuli during each 3.5s silent period was considered a single event. The onsets vector was convolved with a square-wave of the event durations, and this vector of event times and durations was then convolved with a canonical hemodynamic response function to generate the predicted BOLD response timeseries for this regressor. The resulting timeseries was resampled without filtering to include only the timepoints during which fMRI data acquisition actually occurred. In contrast to classical approaches to modeling sparse fMRI data, this approach allows for model estimation in which more than one task condition may contribute to the

[3] *SPM8: http://www.fil.ion.ucl.ac.uk/spm/software/spm8/*
[4] *Nipype: http://nipy.org/nipype*
[5] *ART: http://www.nitrc.org/projects/artifact_detect/*

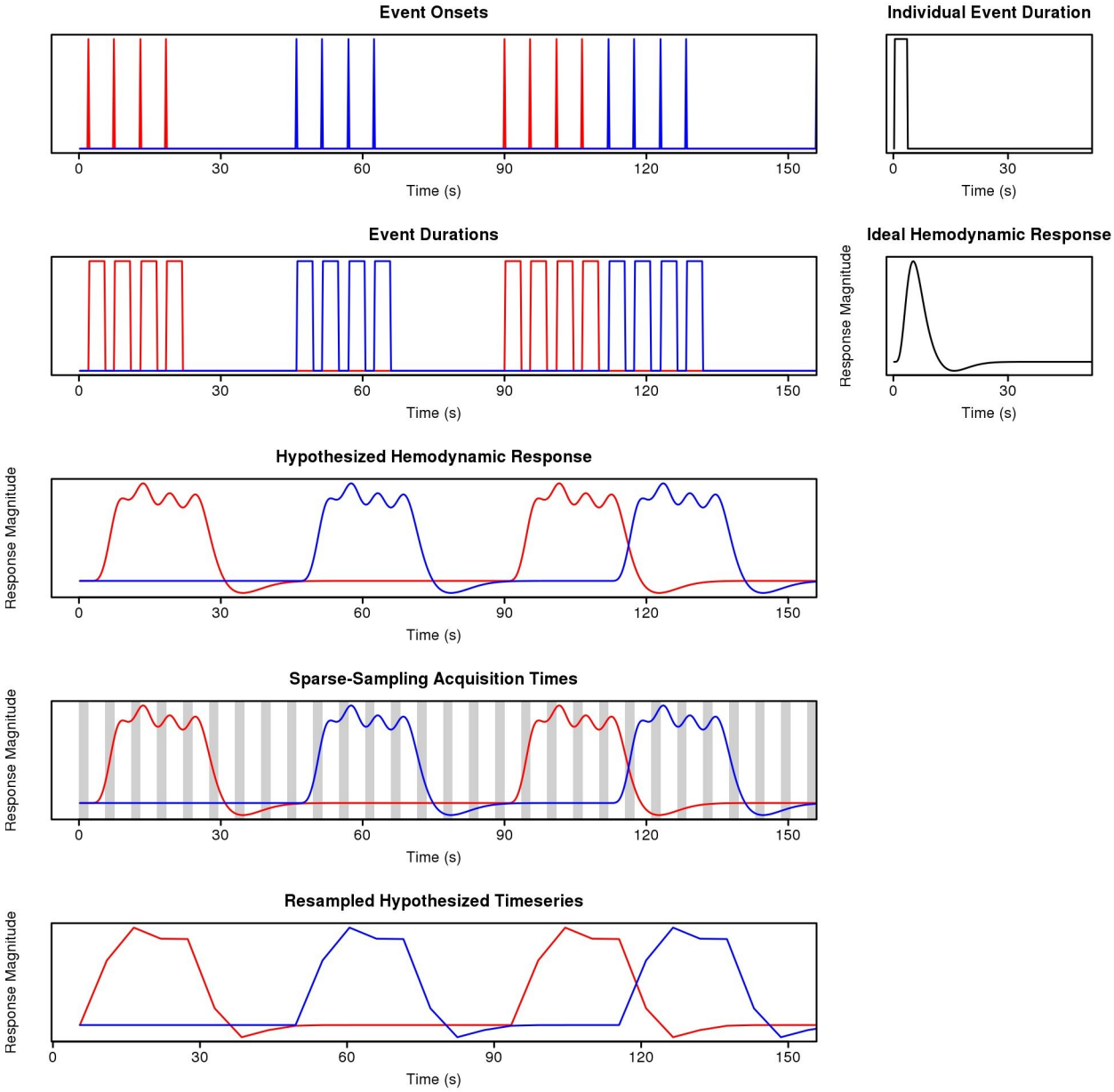

Figure 3.2: Sparse-sampled fMRI model specification. **(a)** For each of the two task conditions (depicted by red and blue lines), a high-temporal resolution vector of event onsets (as delta functions) is convolved with a boxcar function of the event duration. **(b)** The resulting event-duration timeseries is convolved with a canonical hemodynamic response function to produce **(c)** an idealized hypothesized response timeseries. **(d)** This timeseries is resampled at times during which the scanner was actually acquiring data (gray shaded regions) to produce **(e)** the hypothesized response vector for each task condition in the general linear model design matrix.

activity at any given time point. Additionally, this approach affords significantly enhanced functional timecourse estimation via reduced model error compared to classical "boxcar" approaches to sparse fMRI model specification, based on recent computational and empirical assessments carried out by our laboratory (Ghosh *et al.*, 2009; Perrachione, Gabrieli, & Ghosh, 2011).

The coregistration transformation between each participant's mean functional EPI volume and their T1-weighted structural image was calculated using Freesurfer's BBRegister program. The amount of coregistration error did not differ between groups [$F(1,36) = 0.132$, $p = 0.72$]. These transforms were applied to the contrast images from each participant's first-level analysis to insure accurate coregistration between functional data and high-resolution anatomy. Participants' high-resolution structural images were aligned to a common space (the 1mm-isotropic MNI152 template from FSL[6] v4.1.6) using nonlinear symmetric diffeomorphic mapping implemented in ANTS[7] v.1.5 (Avants *et al.*, 2008). The choice of this normalization algorithm was motivated by rigorous comparisons of normalization algorithms (Klein *et al.*, 2009; 2010). The transformation matrix and deformation field from this spatial normalization were applied to each participant's coregistered first-level contrast images to align them to the common space. Second-level group comparisons were performed using SPM8 via Nipype workflows. Group-level statistics were thresholded at $p < 0.05$ and corrected for multiple comparisons via topographic false-discovery rate (FDR) correction at $q = 0.05$. Anatomical locations of functional effects were established using the Harvard-Oxford region atlas from FSL. To facilitate visualization of whole-brain effects, the results of these volume-based second-level analyses have been projected to the cortical surface using Freesurfer.

[6] *FSL: http://www.fmrib.ox.ac.uk/fsl/*
[7] *ANTS: http://www.picsl.upenn.edu/ANTS/*

3.3 Results

3.3.1 Task-related activation

An extensive collection of cortical and subcortical areas demonstrated task-related activation, including bilateral superior temporal gyrus (STG; including Heschl's gyrus and planum temporale), angular gyrus, middle frontal gyrus (MFG), inferior frontal gyrus (IFG; both pars triangularis and pars opercularis), precentral gyrus, supplementary motor area (SMA), fusiform gyrus, lateral occipital cortex, basal ganglia, thalamus, and sensory brainstem. Task-related deactivations (greater response during rest blocks) were observed in many regions comprising the brain's "default-mode network" (Buckner, Andrews-Hanna, & Schacter, 2008), including bilateral superior frontal gyrus, temporal pole and anterior middle temporal gyrus (MTG), lateral inferior parietal lobe, hippocampus, paracingulate cortex (medial prefrontal cortex), anterior and posterior cingulate cortex, cuneus, precuneus, lingual gyrus, and right postcentral gyrus.

The pattern of task-activated and deactivated regions was the same across the control and dyslexia groups. There were no statistically significant differences between the control and dyslexia groups in regions exhibiting task-related activity. The dyslexia group did exhibit significantly greater task-related deactivations in bilateral lingual gyrus, posterior cingulate, precuneus, and left inferior lateral parietal lobe / posterior MTG than the control group.

3.3.2 Adaptation to the phonetic consistency of a single talker

Participants in the control group exhibited widespread adaptation to speech produced by a single, consistent talker versus multiple talkers throughout cortical regions implicated in speech processing (Hickok & Poeppel, 2007), as shown in Fig. 3.3a. In particular, significant adaptation to speech from a consistent talker was observed bilaterally in superior temporal gyrus (STG), including Heschl's gyrus (HG) and planum temporale (PT), and extending into posterior middle temporal gyrus (MTG) and inferior supramarginal gyrus (SMG). Adaptation was also observed bilaterally in ventral premotor

cortex and inferior frontal gyrus (IFG) pars opercularis.

The dyslexia group also exhibited significant adaptation in bilateral STG, though its magnitude and extent was reduced compared to controls (Fig 3.3b). Unlike the control group, regions of significant adaptation did not extend into posterior MTG or inferior SMG, nor were significant clusters of adaptation observed in premotor cortex or IFG.

In both the control and dyslexia groups, a number of task-activated areas were not differentially activated between the No-Adaptation and Adaptation conditions, including brainstem, thalamus, basal ganglia, dorsal precentral gyrus, supplementary

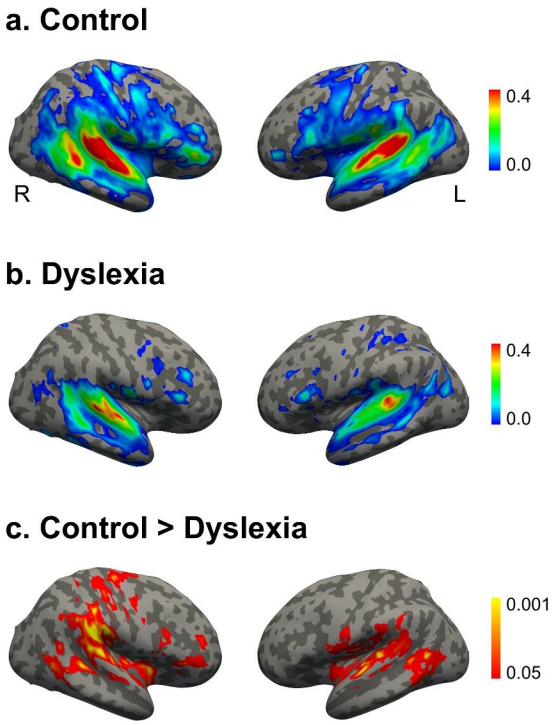

Figure 3.3: Adaptation to phonetic consistency during speech perception. Individuals with dyslexia exhibited significantly diminished neural adaptation to the consistent phonetic properties of spoken language. Compared to speech produced by multiple, unpredictable talkers, speech produced by a single talker elicited widespread adaptation bilaterally throughout superior and middle temporal cortex in the control group, but the magnitude and extent of this adaptation was significantly less in the dyslexia group. **(a,b)** Within-group figures show the magnitude of adaptation (effect size of the No-Adaptation > Adaptation contrast) in each group. **(c)** Between-groups contrast shows regions where individuals with dyslexia exhibit significantly less adaptation than controls ($p < 0.05$, cluster-corrected FDR $p < 0.05$).

motor area (SMA), IFG pars triangularis, and ventral visual cortices; nor was there a difference in default-mode network deactivations. This suggests adaptation in auditory and association cortices is not epiphenomenal with respect to participants' state between the two conditions, but is specifically related to auditory language processes differentially engaged in accommodating phonetic variability versus consistency.

A direct comparison of the voxelwise magnitude of adaptation between the control and dyslexia groups revealed a significant reduction in auditory adaptation in the dyslexia group across an extensive cortical area (Fig. 3.3c). The dyslexia group exhibited significantly less adaptation in bilateral STG, including HG and PT, bilateral MTG, right IFG, and bilateral inferior SMG. The nature of this group difference was due to a larger and more consistent reduction in activity to the adapted talker vs. multiple talkers in the control group than in the dyslexia group. There were no regions in which the magnitude of adaptation in the dyslexia group significantly exceed that of the control group.

In addition to an overall group difference in the magnitude of adaptation, we investigated whether, within the dyslexia group, individual differences in reading ability and auditory cortical adaptation were related. The mean adaptation magnitude to phonetic consistency in auditory cortical areas was extracted for each participant in the dyslexia group based on the probabilistic location of Heschl's gyrus in the Harvard-Oxford brain atlas. These values were submitted to a linear mixed effects model in R[8] as a random factor, with participant as a fixed factor, to test the alternative hypothesis that adaptation magnitude was positively linearly related to participants' reading ability as measured by the "Word Attack" subtest of the *Woodcock Reading Mastery Test* (Woodcock, 1998). Performance on this test was chosen as an index of reading proficiency because it "measures [the] ability to apply phonic and structural analysis skills to pronounce unfamiliar words," and thus captures both the phonological and orthographic decoding components of skilled reading. This model revealed a significant relationship between

[8] *R: http://www.r-project.org/*

participants' reading ability and the magnitude of adaptation to speech stimulus consistency [$t(15) = 1.90$, $p < 0.04$], as shown for left auditory cortex in Fig. 3.4. Similar results obtain in planum temporale and in corresponding right hemisphere regions.

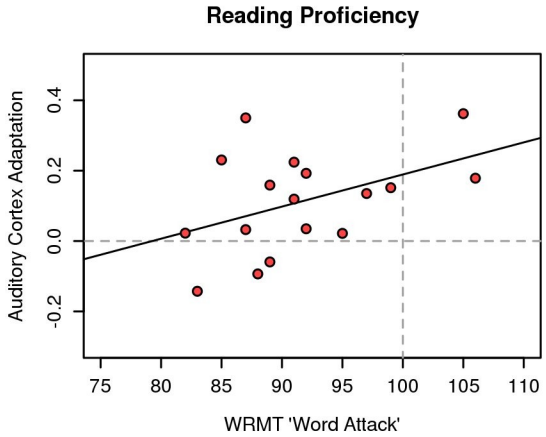

Figure 3.4: Magnitude of adaptation in auditory cortices is related to out-of-scanner behavioral measures of reading ability in dyslexia. Reading proficiency, as measured by the 'Word Attack' subtest of the *Woodcock Reading Mastery Test*, is significantly positively related to the magnitude of adaptation in posterior auditory cortices. Individuals with dyslexia scoring higher on behavioral measures of reading ability tended to have greater adaptation in auditory cortical areas, whereas those exhibiting greater behavioral reading impairment also exhibited reduced neural adaptation to auditory stimulus consistency. The regression is indicated by the solid line; lighter dashed lines indicate the normalized population mean performance on the reading assessment, and zero adaptation (no physiological response difference between repeated and unrepeated stimuli).

3.4 Discussion

In this experiment we observed that the presentation of speech from a single, consistent talker resulted in a reduction in the hemodynamic response in auditory language areas compared to speech from multiple talkers, presumably reflecting perceptual adaptation while attending to the speech of the single talker. The observed physiological correlates of talker adaptation are generally consistent with previous reports of auditory adaptation during speech perception (Belin & Zatorre, 2003; Wong, Nusbaum, & Small, 2004; Chandrasekaran, Chan, & Wong, 2011).

With respect to our hypothesis, there was also a significant difference between the control and dyslexia groups in terms of the magnitude of neural adaptation to speech of an individual talker. Compared to typically-reading controls, individuals with dyslexia exhibited significantly reduced neural adaptation, presumably reflecting differential sensitivity to phonetic consistency between the two groups and consistent with the hypothesis that the ability to learn short-term phonetic consistency is impaired in dyslexia. These group differences in adaptation were observed specifically in the same task-activated auditory language areas that exhibited adaptation within each group, further suggesting that the observed effect is related specifically to the diminished ability of dyslexic participants' auditory cortices to dynamically construct the short-term representations of phonetic consistency associated with talker adaptation. Moreover, we observed that the magnitude of adaptation in auditory cortices in the dyslexia group was significantly and positively related to their reading ability, such that individuals exhibiting the least adaptation were also those with weakest reading skills.

All together, the results from Experiment 2 are consistent with the hypothesis that individuals with dyslexia are impaired in the ability to learn the short-term patterns of phonetic consistency during speech perception that are necessary precursors to developing robust, long-term representations of phonological categories. These results are further consistent with the hypothesis that this difficulty in learning is specifically related to the diminished capacity plasticity mechanisms in sensory cortex to develop the dynamic representations of stimulus consistency associated with neural adaptation.

4. Generalized neural adaptation deficits in dyslexia

Neural systems facilitate perception by rapidly adapting to repeated, predictable features of the environment. Such perceptual facilitation for repeated relative to novel percepts is associated with rapid cortical plasticity in animal models and with reduced hemodynamic response in neuroimaging studies. Individuals with dyslexia often exhibit behavioral impairments in tasks where stimulus consistency typically enhances perception. We compared neural adaptation between typical and dyslexic young adults in multiple domains, including both auditory and visual, linguistic and non-linguistic stimuli. Compared with controls, individuals with dyslexia demonstrated significantly reduced neural adaptation to every stimulus category assessed, revealing a broad dysfunction of rapid neural adaptation independent of either sensory modality or linguistic processing. Diminished neural adaptation may indicate an underlying, generalized dysfunction of rapid cortical plasticity in this disorder. Such a deficit would impair perceptual category learning, which is critical to the development of robust phonological and orthographic categories that are the basis for reading expertise.

4.1 Introduction

Learning depends upon rapid, dynamic, and short-term neural plasticity to meet time-varying task demands (Jääskeläinen *et al.*, 2007). In particular, neural systems adapt to consistent, predictable information about the stimulus environment to facilitate perception. The ability to dynamically adjust perceptual representations begins with transient changes to the receptive fields of neurons in sensory cortex (Fritz *et al.*, 2003;

Edeline, Pham, & Weinberger, 1993; Froemke, Merzenich, & Schreiner, 2007; Lee & Middlebrooks, 2011), which are associated with enhanced ability to detect stimuli (Atiani *et al.*, 2009; Ahveninen *et al.*, 2011). If the behavioral relevance of these transient changes persists, longer-term changes are seen in the organization of respective cortical maps (Suga *et al.*, 2002; Dinse *et al.*, 2003), which may be a necessary component of long-term perceptual category learning (Alain *et al.*, 2007; Adab & Vogels, 2011; Reed *et al.*, 2011).

Although the mechanisms of rapid plasticity that facilitate long-term learning are known principally from work in animal models, the same class of mechanisms likely also supports human perceptual learning. Learning to read, in which visual symbols are learned and related to auditory representations associated with language, is one of the most remarkable and complex examples of such human learning. The demands of learning to read are evident from its lengthy and explicit educational instruction. Some individuals struggle in learning to read due to developmental dyslexia, a neurological condition that impairs the acquisition of reading skill, despite adequate intelligence, motivation, and educational opportunities (Lyon, Shaywitz, & Shaywitz, 2003; Gabrieli, 2009). In alphabetic orthographies like English, deficits in phonological processing – impaired representation of, or access to, the abstract units of spoken language – have been implicated as the principal source of reading difficulties in dyslexia (Bradley & Bryant, 1983; Vellutino *et al.*, 2004) independent of other cognitive factors (Tanaka *et al.*, 2011).

In addition to a core phonological deficit and concomitant reading impairment, individuals with dyslexia exhibit perceptual deficits in tasks that may involve neither reading nor language, but in which adaptation-related processes enhance the perceptual performance of typical readers. In a frequency-discrimination paradigm, typical readers demonstrate enhanced perceptual thresholds when one of the two tones in each pair is held constant throughout the experiment, whereas no such perceptual enhancement is obtained in individuals with dyslexia (Ahissar *et al.*, 2006). Frequency-discrimination

training results in rapid changes to the receptive fields of individual neurons (Fritz *et al.*, 2003; Edeline, Pham, & Weinberger, 1993) and the organization of auditory cortical maps (Recanzone, Schreiner, & Merzenich, 1993; Rutkowski & Weinberger, 2005) with respect to the learned tones. Likewise, a number of studies have shown that the addition of noise is significantly more detrimental to individuals with dyslexia than controls for both auditory and visual, verbal and non-verbal perceptual tasks (Sperling *et al.*, 2005, 2006; Ziegler *et al.*, 2009; Chait *et al.*, 2007). In auditory cortex, the perception of stimuli in noise is facilitated by simultaneous enhancement of the neural circuits sensitive to features of the target stimulus and inhibition of those sensitive to features of the noise (Atiani *et al.*, 2009; Ahveninen *et al.*, 2011). Overall, the range of tasks evincing perceptual deficits in dyslexia appears to be those in which consistent contextual information implicitly guides perceptual performance in typically developing readers (Banai & Ahissar, 2010).

Given the close correspondence between adaptation-related perceptual impairments in dyslexia and behaviors known to be supported by rapid sensory cortical plasticity, we hypothesized that rapid cortical plasticity may be dysfunctional in individuals with lifelong history of reading difficulty. To interrogate rapid cortical plasticity in healthy human brains, we developed a series of experiments employing functional magnetic resonance imaging (fMRI) adaptation (Grill-Spector & Malach, 2001; Krekelberg, Boynton, & van Wezel, 2006). In these paradigms, the repetition of a stimulus typically results in a reduction of blood oxygenation level dependent (BOLD) signal in cortex containing neurons sensitive to that stimulus type (Weiner *et al.*, 2010; Bell *et al.*, 2011).

In Experiments 3a-d, we investigated the scope and limits of the reduced plasticity observed for consistent speech phonetics in Experiment 2. We measured differences in the fMRI BOLD signal resulting from sequences of unique, novel stimuli ("No-Adaptation" condition) versus multiple repetitions of a single stimulus ("Adaptation" condition) for auditory words (Experiment 3a), visual words (Experiment 3b), visual objects

(Experiment 3c), and faces (Experiment 3d). We hypothesized that individuals with dyslexia would exhibit reduced adaptation for auditory words, consistent with their reduced adaptation for a talker in Experiment 2. We also hypothesized that the reduced adaption would extend to printed words, due to the relation between auditory language and visual processes that underlie learning to read. The inclusion of objects and faces allowed for a determination of the scope of the reduced adaptation. If reduced adaptation is specific to auditory and visual systems associated with language and reading, then individuals with dyslexia would exhibit typical adaptation for objects and faces. If reduced adaptation is a more general feature of dyslexia, then reduced adaptation would extend to non-linguistic stimuli. Ultimately, we observed deficient fMRI adaptation to perceptual consistency in dyslexia for every stimulus type assessed (speech phonetics, auditory words, visual words, visual objects, and faces), suggesting that a dysfunction of rapid cortical plasticity may be fundamental to dyslexia.

4.2 Methods

4.2.1 Participants

Two groups of adult participants were recruited for this study: (*1*) individuals with a prior dyslexia diagnosis or lifelong history of reading difficulties (N = 23), and (*2*) controls (N = 24), who had a self-reported history free from reading difficulty. All subjects were native speakers of American English and had a self-reported history free from additional language, speech, or peripheral hearing disorders, and reported no other known psychological or neurological disorders. The sample in Experiment 3 was unique from that of Experiment 2, with the exception of three controls and five individuals with dyslexia who participated in both. Analyses of some fMRI runs in Experiment 3 were rejected due to excessive participant motion or other artifacts, such that in Experiment 3a: N = 21 control, 21 dyslexia; Experiment 3b: N = 23 control, 23 dyslexia; Experiment 3c: N = 23 control, 23 dyslexia; Experiment 3d: N = 22 control, 22 dyslexia.

		Control		Dyslexia		
Test	Subtest	Raw Score	Standard Score	Raw Score	Standard Score	Cohen's *d*
WASI						
	Block Design	59.7 ± 8.5	60.7 ± 5.6	54.3 ± 14.8	57.4 ± 9.7	0.425
	Matrix Reasoning	30.7 ± 4.6	61.0 ± 14.4	30.9 ± 4.4	61.0 ± 14.7	0.007
	Performance IQ	118.9 ± 9.4	116.0 ± 9.1	115.7 ± 13.3	113.6 ± 12.0	0.234
CTOPP						
	Elision	19.3 ± 0.9	11.3 ± 0.9	16.3 ± 3.1	8.7 ± 2.1	1.703
	Blending Words	18.2 ± 1.1	12.0 ± 1.4	14.4 ± 3.5	9.0 ± 2.7	1.412
	Non-word Repetition	14.2 ± 1.7	10.5 ± 2.5	10.8 ± 2.5	7.3 ± 1.2	1.679
RAN						
	Numbers	16.2 ± 3.1	113.6 ± 5.4	23.9 ± 11.4	100.7 ± 13.5	1.281
	Letters	16.2 ± 3.1	113.6 ± 5.4	23.9 ± 11.4	100.7 ± 13.5	1.281
	Numbers & Letters	16.3 ± 3.1	110.7 ± 4.8	23.3 ± 6.9	100.6 ± 11.0	1.225
WRMT-R/NU						
	◊ Word ID	100.5 ± 3.3	109.7 ± 9.3	88.1 ± 7.3	89.7 ± 8.6	2.291
	◊ Word Attack	39.1 ± 3.3	107.9 ± 13.8	29.5 ± 4.8	87.0 ± 6.0	1.994
	Passage Comprehension	17.9 ± 4.0	115.8 ± 8.0	26.2 ± 7.7	101.4 ± 10.6	1.580
TOWRE						
	◊ Sight Word Reading	100.2 ± 5.1	106.5 ± 8.5	77.2 ± 16.0	84.0 ± 10.9	2.369
	◊ Decoding	58.4 ± 2.7	107.9 ± 7.8	32.7 ± 10.9	76.7 ± 10.6	3.430
	Total	214.4 ± 11.6	108.6 ± 7.1	159.5 ± 19.8	75.7 ± 11.8	3.494
WJIII						
	Fluency	104.8 ± 22.1	123.3 ± 17.4	70.9 ± 16.4	98.0 ± 11.9	1.697
WAIS-IV						
	Digit Span Total	32.6 ± 5.1	12.3 ± 2.8	24.6 ± 3.8	8.1 ± 1.9	1.776
Age (years)		22.3 ± 3.4		22.3 ± 4.4		0.003
Education (years)		15.5 ± 1.7		14.9 ± 1.9		0.318
Sex		12 M / 12 F		4 M / 19 F		0.299 (φ)

Table 4.1: Cognitive, behavioral, and demographic assessment of participants in Experiment 3. Values are mean ± standard deviation. Cohen's *d* shows the effect size of the group difference in standard scores. Diamonds (◊) denote tests used as inclusionary/exclusionary criteria for group membership. Abbreviations: WASI: *Wechsler Abbreviated Scale of Intelligence*, 3rd Ed. (Wechsler, 2008); CTOPP: *Comprehensive Test of Phonological Processing* (Wagner, Torgesen, & Rashotte, 1999); WRMT-R/NU: *Woodcock Reading Mastery Test-Revised* (Woodcock, 1998); TOWRE: *Test of Word Reading Efficiency* (Torgesen, Wagner, & Rashotte, 1999); WAIS-IV: *Wechsler Adult Intelligence Scale* (Wechsler, 1999).

To confirm participants' status as typical or impaired readers, their performance on a battery of standardized intelligence, memory, reading, and phonological measures was assessed. Performance at or below the 25th percentile on two or more subtests of timed or untimed word or nonword reading comprised inclusionary criteria for the dyslexia group. Performance at or below the 25th percentile on any one such subtest

comprised exclusionary criteria from the control group. All participants scored at or above average on measures of performance IQ and working memory. Enumeration of the specific assessments used, as well as group average performance on these measures and basic demographics, are reported in Table 4.1.

4.2.2 Stimuli

4.2.2.1 Experiment 3a – Spoken Words

Audio stimuli consisted of 180 monosyllabic nouns read in isolation by one adult female native-English speaker and were recorded in a sound-attenuated chamber via a SHURE SM58 microphone. Stimuli were sampled at 44.1 kHz using an Edirol UA-25EX sound card, and normalized for RMS amplitude to 70 dB SPL using Praat[1] (Boersma, 2001). Normalized stimuli were spectrally filtered to attain frequency response equalization for binaural presentation via a pair of Sensimetrics (Malden, MA) S-14 MRI-compatible insert earphones. Recordings of words were 234-591ms in duration (M = 425ms, SD = 66ms). 160 words were assigned to the "No-Adaptation" condition, and 20 were assigned to the "Adaptation" condition. Target stimuli consisted of 20 items from each condition whose recordings were time-reversed using Praat.

4.2.2.2 Experiment 3b – Written Words

Orthographic stimuli consisted of 180 monosyllabic nouns, written in bold 18 pt Arial font on a white background of 256×256 pixels at 72dpi. Words were 3-5 letters in length (mode = 4). 160 words were assigned to the "No-Adaptation" condition, and 20 were assigned to the "Adaptation" condition. Target stimuli consisted of 20 trials in each condition in which the images were vertically inverted.

4.2.2.3 Experiment 3c – Objects

Visual object stimuli consisted of 180 color photographs of individual objects in

[1] *Praat: http://www.fon.hum.uva.nl/praat/*

isolation on a white background, 256×256 pixels at 72dpi. Only objects with unambiguous vertical orientations were selected (*e.g.*, a car or tree, not a pencil or grapefruit). 160 objects were assigned to the "No-Adaptation" condition, and 20 were assigned to the "Adaptation" condition. Target stimuli consisted of 20 trials in each condition in which the images were vertically inverted.

4.2.2.4 Experiment 3d – Faces

Faces stimuli consisted of 180 greyscale photographs of individuals, cropped close to the face without excessive hair or backgrounds, and were 256×256 pixels at 72dpi. 160 faces were assigned to the "No-Adaptation" condition, and 20 were assigned to the "Adaptation" condition. Target stimuli consisted of 20 trials in each condition in which the images were vertically inverted.

4.2.3 Procedure

4.2.3.1 Experiment 3a – Spoken Words

Participants lay supine in an MRI scanner and undertook two runs of an auditory deviant-detection task during continuous-sampling fMRI. Each run consisted of 10 blocks of the "Adaptation" condition, in which the same auditory word was presented 8 times in succession; 10 blocks of the "No-Adaptation" condition, in which 8 different words were presented; and 10 blocks of rest. During the task, participants were asked to fixate on a white "+" symbol in the center of the screen, which dimmed slightly during rest blocks to indicate no auditory stimuli were to be expected. The projector background remained at 31.25% luminance throughout the experiment. Auditory stimuli were presented binaurally in blocks of 8 with a duration of 1200ms between the onset of subsequent stimuli. One stimulus in each block was time-reversed; participants indicated detection of these deviant stimuli by button press (Fig. 4.1a,b).

4.2.3.2 Experiment 3b-d – Written Words, Objects, and Faces

Participants completed two runs each of the three visual stimulus categories. For

each of these tasks, participants lay supine in an MRI scanner and performed a visual deviant-detection task during continuous-sampling fMRI. Each run consisted of 10 blocks of the "Adaptation" condition, in which the same visual stimulus was presented 8 times in succession; 10 blocks of the "No-Adaptation" condition, in which 8 different stimuli were presented; and 10 blocks of rest. During the task, visual stimuli were presented in blocks of 8. Each stimulus remained on the screen for 700ms, with a 500ms inter-trial interval between subsequent stimuli. One stimulus in each block was vertically inverted; participants indicated detection of these deviant stimuli by button press (Fig. 4.1c-h). During rest blocks, participants were asked to fixate on a white "+" symbol in the center of the screen and wait for the images to begin again. The projector background remained at 31.25% luminance throughout the experiment.

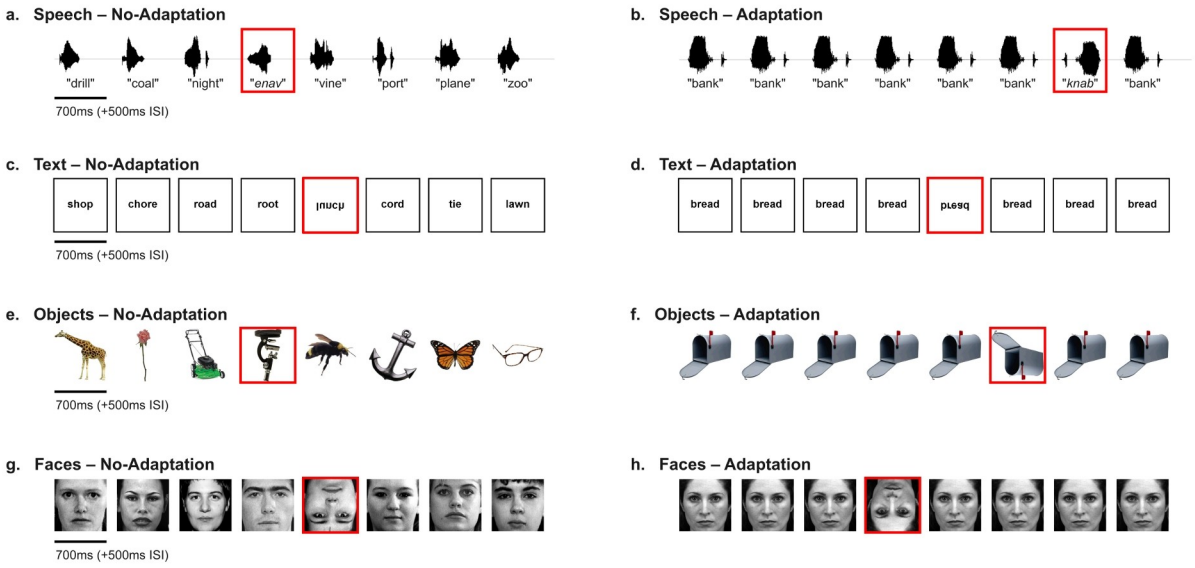

Figure 4.1: Design of stimulation paradigms in Experiment 3. **(a)** Participants detected a deviant auditory stimulus (spoken words) which was time-reversed, under two conditions: a block of multiple, different words, or **(b)** a block of a single word repeated eight times. **(c,d)** Adaptation to text was measured by the presentation of multiple, different written words versus a single, repeated one. **(e,f)** Adaptation to visual objects was measured by the presentation of multiple, different object photographs versus a single, repeated one. **(g,h)** Adaptation to faces was measured by the presentation of multiple, different face photographs versus a single, repeated one. In all visual tasks in Experiment 3, participants detected a deviant (vertically inverted) stimulus, indicated here in red outline.

4.2.4 MRI Data Acquisition

Data were acquired on a Siemens Trio 3T scanner with a 32-channel phased array head coil. A whole-head, high-resolution T1-weighted multi-echo MPRAGE anatomical volume (acquisition parameters: TR = 2350ms, TE = {1.79ms, 3.71ms, 5.63ms, 7.55ms}, TI = 1400ms, flip angle = 7°, FOV = 256 × 256, 176 slices, voxel resolution = 1.0 × 1.0 × 1.0mm) was acquired at the beginning of each session.

Two functional runs containing 146 volumes each were collected for each of the four stimulus types (speech, text, objects, and faces) using continuously-sampled T2*-weighted EPI scans (acquisition parameters: TR = 2000ms, TE = 30ms, flip angle = 90°, voxel resolution = 3.0 × 3.0 × 3.0mm, FOV = 64 × 64, 32 transverse slices providing whole-brain coverage). Each run was preceded by the five additional TRs from which no data were recorded to allow for stabilization of longitudinal magnetization.

4.2.5 MRI Data Analysis

Cortical reconstruction and parcellation of anatomical images was performed using the default processing stream Freesurfer[2] v5.0.0 (Dale *et al.*, 1999). Functional data were analyzed in SPM8[3] using workflows in Nipype[4] v0.4 (Grogolewski *et al.*, 2011). Image preprocessing consisted of motion correction (rigid-body realignment to the mean EPI image from the first functional run) and spatial smoothing (6mm isotropic FWHM 3D Gaussian kernel). Motion and intensity outliers (functional volumes exceeding 1mm in differential motion or differing from the mean image intensity by > 3 SD) were identified using ART[5] and regressed out of the hypothesized timeseries. The number of regressed outliers did not differ between the two groups in any of the 4 stimulus conditions [$F(1,46) = 0.02$, $p = 0.88$]. Model design was implemented using the modelgen algorithm in Nipype, and included, for each run, two task regressors (for the No-Adapta-

[2] *Freesurfer: http://surfer.nmr.mgh.harvard.edu/*
[3] *SPM8: http://www.fil.ion.ucl.ac.uk/spm/software/spm8/*
[4] *Nipype: http://nipy.org/nipype*
[5] *ART: http://www.nitrc.org/projects/artifact_detect/*

tion and Adaptation conditions, respectively), six motion parameters, individual regressors for any outlier volumes, two Legendre polynomial terms to account for low-frequency components of the MR-signal including scanner drift, and a constant term. Within-subject estimation of the general linear model and contrasts were conducted in participants' native EPI space.

The coregistration transformation between each participant's mean functional EPI volume and their T1-weighted structural image was calculated using Freesurfer's BBRegister program. The amount of coregistration error did not differ between groups for any of the 4 tasks [$F(1,46) = 0.46$, $p = 0.50$]. These transforms were applied to the contrast images from each participant's first-level analysis to insure accurate coregistration between functional data and high-resolution anatomy. Participants' high-resolution structural images were aligned to a common space (the 1mm-isotropic MNI152 template from FSL[6] v4.1.6) using nonlinear symmetric diffeomorphic mapping implemented in ANTS[7] v.1.5 (Avants *et al.*, 2008). The choice of this normalization algorithm was motivated by rigorous comparisons of normalization algorithms (Klein *et al.*, 2009; 2010). The transformation matrix and deformation field from this spatial normalization were applied to each participant's coregistered first-level contrast images to align them to the common space. Second-level group comparisons were performed using SPM8 via Nipype workflows. Group-level statistics were thresholded at $p < 0.05$ and corrected for multiple comparisons via topographic false-discovery rate (FDR) correction at $q = 0.05$. Anatomical locations of functional effects were established using the Harvard-Oxford region atlas from FSL.

[6] *FSL: http://www.fmrib.ox.ac.uk/fsl/*
[7] *ANTS: http://www.picsl.upenn.edu/ANTS/*

4.3 Results

4.3.1 Experiment 3a: Spoken Words

4.3.1.1 Task-related activation

An extensive collection of cortical and subcortical areas demonstrated task-related activation, including bilateral superior temporal gyrus (STG; including Heschl's gyrus and planum temporale), posterior supramarginal gyrus, inferior frontal gyrus (IFG; both pars triangularis and pars opercularis), precentral gyrus, putamen, thalamus, sensory brainstem, and medial posterior cerebellar hemispheres. Task-related deactivations (greater response during rest blocks) were more extensive than in Experiment 2, and were observed both in visual areas (including intra- and supracalcarine cortex, lateral occipital cortex, fusiform gyrus, and lingual gyrus) and in regions of the default-mode network, including bilateral superior frontal gyrus, anterior middle temporal gyrus (MTG), lateral inferior parietal lobe, hippocampus, paracingulate cortex (medial prefrontal cortex), anterior and posterior cingulate cortex, cuneus, precuneus, and postcentral gyrus (especially on the right).

The pattern of task-activated and deactivated regions were highly similar between the control and dyslexia groups. There were no statistically significant differences between the control and dyslexia groups in cortical or subcortical regions exhibiting task-related activity. The dyslexia group exhibited significant activation of the cerebellar vermis, whereas the control group did not, and this difference was significant; the dyslexia group also exhibited significantly less deactivation of lingual gyrus compared to controls.

4.3.1.2 Adaptation to repetition of spoken words

Participants in the control group exhibited widespread adaptation to the repetition of a single auditory word versus multiple, different words (all spoken by the same talker) as shown in Fig. 4.2a. These regions closely paralleled those from Experiment 2, including bilateral STG, left PT, and posterior MTG, though also extending further into

anterior MTG. Significant adaptation was also observed in bilateral IFG pars triangularis (*cf.* Experiment 2), orbitofrontal cortex, anterior cingulate gyrus, fusiform gyrus, inferior lateral occipital cortex (LOC), hippocampus, and putamen.

The dyslexia group also exhibited areas of significant adaptation in bilateral superior temporal lobe, though primarily restricted to anterior superior temporal sulcus (STS), which were of reduced magnitude and less posterior or dorsal extent than in the control group (Fig. 4.2b). Adaptation was also seen bilaterally in IFG pars triangularis and orbitofrontal cortex.

In both the control and dyslexia groups, significant enhancement (greater activation following multiple repetitions of a single word) was seen in left anterior SMG. The

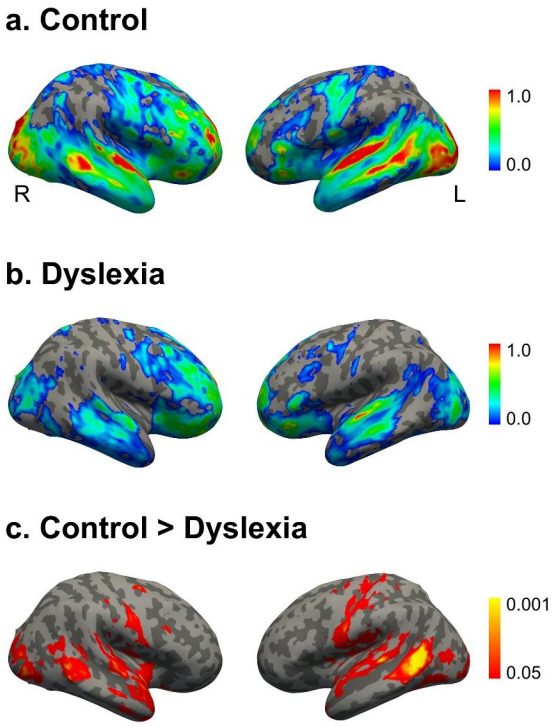

Figure 4.2: Adaptation to auditory (spoken) words. **(a,b)** Within-group figures show the magnitude of adaptation (effect size of the No-Adaptation > Adaptation contrast) in each group. Individuals in the control group demonstrated widespread cortical adaptation to repeated auditory words, including in bilateral STG, MTG, and IFG. The magnitude and extent of adaptation was comparatively less in individuals with dyslexia. **(c)** Between-groups contrast shows that individuals with dyslexia exhibited significantly less adaptation than controls in bilateral STG, posterior MTG, and ventral somatomotor cortex. ($p < 0.05$, cluster-corrected FDR $p < 0.05$)

dyslexia group also demonstrated significant enhancement in bilateral HG, whereas adaptation was seen in this region in controls. In both the control and dyslexia groups, adaptation did not extend to other task-activated areas, including right PT, bilateral IFG pars opercularis, and precentral gyrus, nor was there a difference between conditions in default-mode network deactivations.

Compared to the magnitude of adaptation in the control group, the dyslexia group exhibited several regions of significantly reduced adaptation (Fig. 4.2c), including bilateral STG (including HG), left PT, bilateral posterior MTG, fusiform gyrus, central sulcus, and putamen. The nature of this group difference was due to a larger and more consistent reduction in activity to a repeated word vs. multiple unrepeated words in the control group than in the dyslexia group. There were no regions in which the magnitude of adaptation in the dyslexia group significantly exceeded that of the control group.

4.3.2 Experiment 3b: Text

4.3.2.1 Task-related activation

Regions exhibiting significant task-related activity to viewing text including inferior lateral occipital cortex, fusiform gyrus, superior angular gyrus, superior posterior supramarginal gyrus, inferior frontal gyrus (IFG; principally pars opercularis), precentral gyrus, putamen, left caudate. Task-related deactivations (greater response during rest blocks) were extensive and included both in auditory areas (bilateral superior temporal gyrus, including Heschl's gyrus) and in regions of the default-mode network, including bilateral superior frontal gyrus, temporal pole and anterior middle temporal gyrus (MTG), lateral inferior parietal lobe, paracingulate cortex (medial prefrontal cortex), anterior and posterior cingulate cortex, cuneus, precuneus, and postcentral gyrus (especially on the right).

The pattern of task-activated and deactivated regions was similar between the control and dyslexia groups. Additional significant task-related activation was observed in the dyslexia group in supplementary motor area (SMA) and thalamus; activation in

these areas was not seen in the control group, and these group differences were statistically significant. The dyslexia group additionally exhibited significantly greater task-related activation in left IFG and bilateral basal ganglia than the control group. Greater task-related deactivation was observed in bilateral lingual gyrus and supra- and intracalcarine cortex in controls compared to the dyslexia group.

4.3.2.2 Adaptation to repetition of written words

The repetition of a single written word versus multiple, different words resulted in widespread adaptation in the control group, as shown in Fig. 4.3a. Significant adaptation was observed bilaterally in fusiform gyrus, lingual gyrus, inferior LOC, SMA, middle frontal sulcus, sensory brainstem, and basal ganglia. Adaptation in fusiform gyrus, SMA, and middle frontal sulcus exhibited leftward asymmetry. Left-lateralized adaptation was observed in precentral gyrus, IFG (pars triangularis and opercularis), hippocampus, posterior MTG, anterior STS, and posterior STG (including PT).

Adaptation to text in the dyslexia group was pronouncedly reduced in both extent and magnitude (Fig. 4.3b). Here, significant adaptation was limited to left anterior STS, left IFG (pars triangularis and opercularis) and bilateral basal ganglia. Though some adaptation was observed in left fusiform gyrus, it did not reach significance after correcting for multiple comparisons. The dyslexia group also exhibited significant enhancement (greater activation following multiple repetitions of a single word) in bilateral precuneus, right temporooccipital MTG, and right angular gyrus; similar clusters on the left did not reach significance after multiple comparison corrections. Neural enhancement in dyslexia following repeated presentations of text stimuli has been reported previously (Pugh *et al.*, 2008). No significant enhancement was seen in the control group.

Compared to the magnitude of adaptation in the control group, the dyslexia group exhibited several regions of significantly reduced adaptation (Fig. 4.3c), including left PT, left posterior MTG, left fusiform gyrus, right angular gyrus, and bilateral precuneus. These group differences resulted from differences in the magnitude of adaptation be-

tween groups in fusiform gyrus and PT, and a difference in the direction of the repetition effect (adaptation for the control group, enhancement for the dyslexia group) in MTG and angular gyrus. In no location did the magnitude of adaptation in the dyslexia group significantly exceed that of the control group.

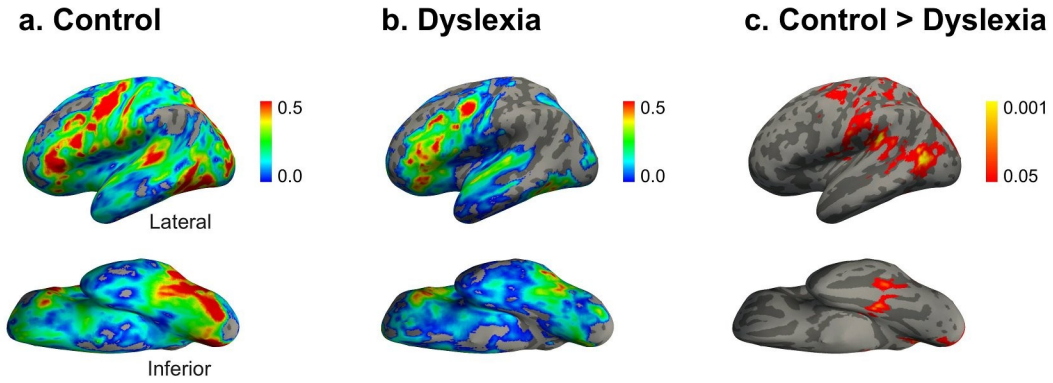

Figure 4.3: Adaptation to repetition of written words (text). **(a,b)** Within-group figures show the magnitude of adaptation (effect size of the No-Adaptation > Adaptation contrast) in each group. Individuals in the control group demonstrated widespread cortical adaptation to repeated visual words, including left IFG, left PT, supramarginal gyrus, fusiform gyrus, ITG, STG, and posterior MTG. The magnitude and extent of adaptation was comparatively less in individuals with dyslexia, especially in posterior regions. In both groups, adaptation to text was strongly left-lateralized. **(c)** Between-groups contrast shows that individuals with dyslexia exhibited significantly less adaptation than controls in left PT, supramarginal gyrus, MTG, and fusiform gyrus. ($p < 0.05$, cluster-corrected FDR $p < 0.05$).

4.3.3 Experiment 3c: Visual objects

4.3.3.1 Task-related activation

Strong activation in response to viewing visual objects was observed throughout visual, frontal, and subcortical brain networks, including: lateral occipital cortex, fusiform gyrus, inferior temporal gyrus, posterior parahippocampal gyrus, orbitofrontal cortex, inferior and middle frontal gyri, supplementary motor area, precentral gyrus, posterior supramarginal gyrus, basal ganglia, thalamus, sensory brainstem, and cerebellar vermis. Task-related deactivations (greater activation during rest blocks) were observed in auditory cortices and the canonical default-mode network, including anterior middle

temporal gyrus, postcentral gyrus (especially on the right), inferior lateral parietal lobe, precuneus, paracingulate (medial prefrontal cortex) and anterior and posterior cingulate cortex.

The pattern of task-related brain activity was highly similar between the control and dyslexia groups. There were no regions in which the control group exhibited greater activation than the dyslexia group. Individuals with dyslexia, meanwhile, exhibited significantly greater task-related activation than controls in left IFG (pars triangularis), bilateral caudate, cerebellar vermis, thalamus, fusiform gyrus, and left posterior MTG.

4.3.3.2 Adaptation to repetition of visual objects

The repetition of a single photograph of an isolated object versus multiple, different objects resulted in the largest and most extensive adaptation of any of the stimulus types. Significant adaptation was observed in the control group bilaterally throughout the visual system, including superior and inferior LOC, intracalcarine cortex, lingual gyrus, fusiform gyrus, posterior inferior temporal gyrus (ITG), parahippocampal gyrus, and thalamus (Fig. 4.4a). Significant adaptation was also observed bilaterally in orbitofrontal cortex, dorsal paracingulate gyrus, medial superior frontal gyrus, middle frontal sulcus, dorsal IFG, superior parietal lobule, putamen, and hippocampus. Regions of task-activated cortex not exhibiting significant adaptation included precentral gyrus, ventral postcentral gyrus, and right posterior MTG. A limited number of regions exhibiting enhancement consisted predominately of task-deactivated regions, including medial prefrontal cortex, posterior cingulate, precuneus, and middle temporal sulcus; this pattern reveals greater deactivation of default-mode network during the No-Adaptation blocks.

Adaptation was observed in the dyslexia group in all the same regions as the control group (Fig. 4.4b), though its magnitude was less. The dyslexia group also exhibited adaptation in two regions the control group did not: medial prefrontal cortex and left middle temporal sulcus. Both of these regions are typically part of the default network,

and both exhibited canonical task-related deactivation in the dyslexia group. The dyslexia group likewise exhibited enhancement in all the same regions as the control group, with the exception of medial prefrontal cortex.

Compared to the magnitude of adaptation in the control group, the dyslexia group exhibited significantly reduced adaptation in superior and inferior LOC (Fig. 4.4c) – the cortical regions shown to be sensitive to physical objects (Malach *et al.*, 1995). The nature of this group difference was due to a larger and more consistent reduction in activity to a repeated object vs. multiple unrepeated objects in the control group than in the dyslexia group. Significantly greater adaptation in the dyslexia group than control was observed in medial prefrontal cortex, right middle temporal sulcus, and right ventral pre-

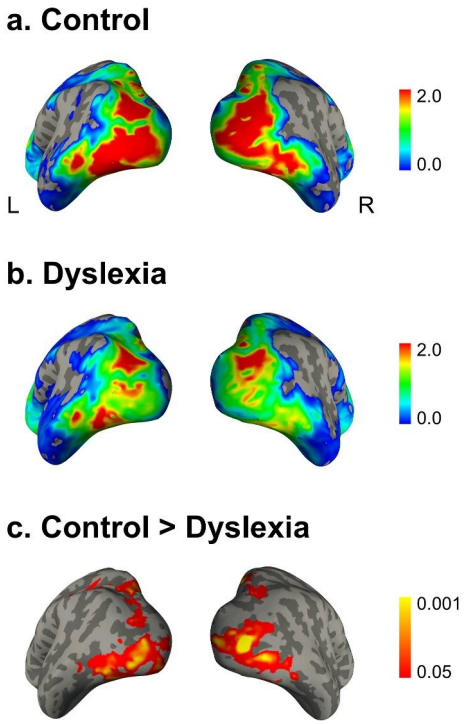

Figure 4.4: Adaptation to repetition of visual objects. **(a,b)** Within-group figures show the magnitude of adaptation (effect size of the No-Adaptation > Adaptation contrast) in each group. Individuals in the control group demonstrated widespread cortical adaptation to repeated visual objects throughout the ventral visual system. Individuals with dyslexia exhibited adaptation in similar regions, though its magnitude was comparatively less. **(c)** Between-groups contrast shows that individuals with dyslexia exhibited significantly less adaptation than controls in inferior LOC bilaterally. ($p < 0.05$, cluster-corrected FDR $p < 0.05$). The posterior surfaces of inflated brains are shown.

central gyrus – all regions exhibiting task-related deactivations in both groups. These results indicate adaptation deficits in dyslexia are not limited to tasks involving overt linguistic processes, but extent to basic visual perceptual tasks, as well.

4.3.4 Experiment 3d: Faces

4.3.4.1 Task-related activation

Like visual objects, viewing faces elicited strong and widespread task-related activation in visual and frontal cortices. Significant task-related activation was observed bilaterally in inferior lateral occipital cortex, fusiform gyrus, orbitofrontal cortex, anterior insula, supplementary motor area, precentral gyrus, basal ganglia, thalamus, sensory brainstem, and right inferior frontal gyrus (IFG). In contrast to other stimulus conditions, significant task-related activation to faces was also seen in hippocampus. Task-related deactivation (greater activation during rest blocks) was observed in canonical default-mode areas, including bilateral superior frontal gyrus, anterior middle temporal gyrus (MTG), lateral inferior parietal lobe, paracingulate cortex (medial prefrontal cortex), anterior and posterior cingulate cortex, cuneus, precuneus, and postcentral gyrus (especially on the right). Deactivation was also observed in supra- and intracalcarine cortex and bilateral auditory cortices.

The pattern of task-related activation to viewing faces was highly similar between the control and dyslexia groups. There were no significant differences in task-activated areas between the two groups. The dyslexia group exhibited significantly greater deactivation than the control group in bilateral auditory areas, posterior cingulate, cuneus, and lingual gyrus.

4.3.4.2 Adaptation to repetition of faces

The repetition of a single photograph of a face versus multiple, different faces likewise resulted in large and extensive adaptation in the control group. Significant adaptation was observed bilaterally throughout the visual system, including fusiform

gyrus, superior and inferior LOC, supra- and intracalcarine cortex, lingual gyrus, and temporal pole (Fig. 4.5a), as well as dorsal left IFG and bilateral putamen. Significant adaptation was also observed bilaterally in hippocampus and amygdala, most prominently in the right hemisphere. Regions of task-activated cortex not exhibiting significant adaptation included right IFG, orbitofrontal cortex, caudate, and sensory brainstem. No regions exhibited significant enhancement in either the control or dyslexia group to repeated face stimuli.

Adaptation to repeated faces in the dyslexia group was of substantially reduced extent and magnitude (Fig. 4.5b). Significant adaptation was observed in the dyslexia group in superior and inferior LOC, fusiform gyrus, lingual gyrus, and ITG. Adaptation was also observed in orbitofrontal cortex, but was not significant following multiple comparisons correction. Regions of task-activated cortex not exhibiting significant adaptation in the dyslexia group included right IFG, occipital pole, superior parietal lobule, bilateral amygdala, and bilateral putamen.

Compared to the magnitude of adaptation in the control group, the dyslexia group exhibited significantly reduced adaptation throughout face-sensitive brain areas (Fig.

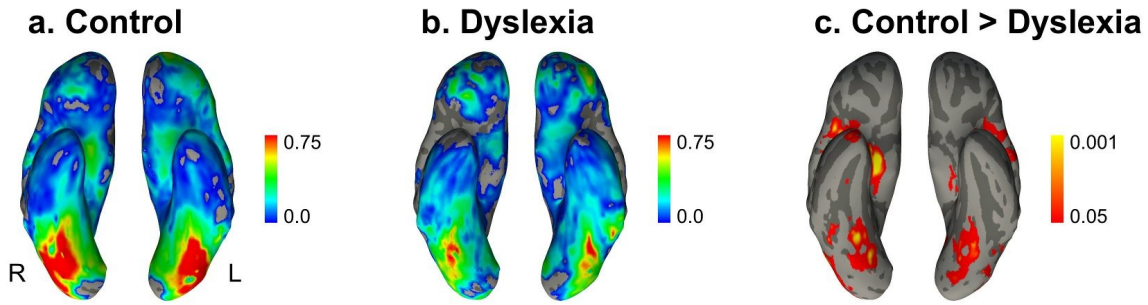

Figure 4.5: Adaptation to repetition of faces. **(a,b)** Within-group figures show the magnitude of adaptation (effect size of the No-Adaptation > Adaptation contrast) in each group. Individuals in the control group demonstrated adaptation to repeated faces in canonical cortical and subcortical face processing areas, including fusiform gyrus, LOC, right hippocampus and amygdala. Individuals with dyslexia exhibited adaptation in similar regions, though its magnitude was comparatively less. **(c)** Between-groups contrast shows that individuals with dyslexia exhibited significantly less adaptation than controls in bilateral fusiform gyrus, LOC, and right amygdala. ($p < 0.05$, cluster-corrected FDR $p < 0.05$). The ventral surfaces of inflated brains are shown.

4.5c), including fusiform gyrus, inferior LOC, temporal pole, and insula (all bilaterally), as well as right amygdala, right hippocampus, and right putamen. The nature of this group difference was due to a larger and more consistent reduction in activity to a repeated face vs. multiple unrepeated faces in the control group than in the dyslexia group. In no location did the magnitude of adaptation in the dyslexia group significantly exceed that of the control group.

To address the possibility that group differences in adaptation are artifactually due to differences in the consistency of localized regions of adaptation effects – rather than differences in the magnitude of adaptation – we further investigated whether the rapid adaptation deficit in the dyslexia group was evident in individually-defined cortical areas selective for face stimuli. The posterior fusiform gyrus is known to contain a region termed the "fusiform face area" (FFA), which exhibits reliably preferential response to faces versus other visual stimuli (Kanwisher, McDermott, & Chun, 1997; Kanwisher & Yovel, 2006). We localized the FFA in each participant individually, and calculated the change in responsiveness of each individual's FFA between the No-Adaptation and Adaptation conditions (Fig. 4.6).

To localize FFA in individual participants, an additional, separate analysis of the data from Experiment 3 was performed in which all four tasks (eight fMRI runs) were included in first-level design matrix of the general linear model for each subject. Model design and estimation otherwise remained as described in §4.2.5. The FFA was localized in individual participants by contrasting activation to faces vs. activation to objects and words and visually identifying the anterior-most discrete face-selective cluster in the occipitofusiform region. The FFA was successfully localized in 22 participants in the dyslexia group and 18 participants in the control group. The probability of localizing an FFA did not differ by group [$\chi^2 = 0.63$, $p = 0.43$, *n.s.*] The control and dyslexia groups did not differ with respect to the threshold (p-value) at which a discrete FFA cluster could be localized [two-tailed independent-sample t-test, $t(38) = 0.06$, $p = 0.95$, *n.s.*], nor in the volume of the FFA [two-tailed independent-sample t-test, $t(38) = 0.65$, $p =$

0.52, *n.s.*], suggesting no difference in the selectivity of cortex specialized for faces between the two groups. This is consistent with previous neuroimaging studies of visual processing in dyslexia that find no difference visual activity related to viewing faces (Brachacki, Fawcett, & Nicolson, 1994; Rüsseler, Johannes, & Munte, 2003; Smith-Spark & Moore, 2009). For each participant, the mean effect size of all voxels within the FFA was computed from the Adaptation and No-Adaptation conditions of the original analysis.

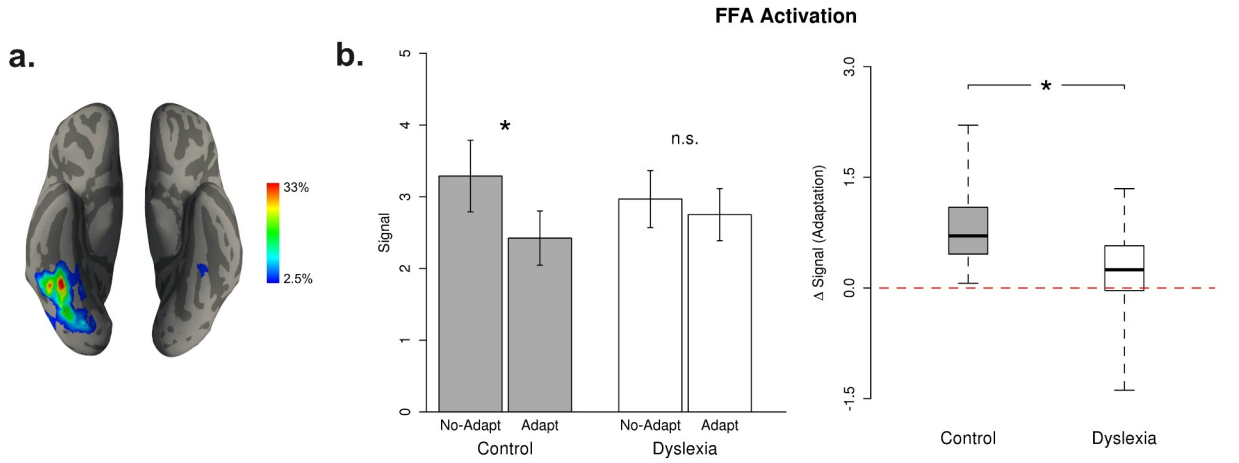

Figure 4.6: Reduced adaptation to repeated faces in face-selective cortex in dyslexia. **(a)** The probabilistic location of the FFA across participants in this sample is shown. **(b)** The control group showed a significant reduction of activation in the Adaptation condition relative to the No-Adaptation condition, whereas in the dyslexia group adaptation in face-selective cortex was not significant. The magnitude of adaptation in participants' individual FFA was significantly less in the dyslexia group than the control group.

The magnitude of adaptation observed in the dyslexia group was again significantly reduced compared to the control group in brain areas identified specifically for their selectivity for face stimuli. The control group showed a significant reduction of activation in the Adaptation condition relative to the No-Adaptation condition within the FFA [two-tailed paired t-test, $t(17) = 6.13$, $p < 1.2 \times 10^{-5}$], whereas adaptation in face-selective cortex was not significant in the dyslexia group [two-tailed paired t-test, $t(21) = 1.67$, $p = 0.11$, *n.s.*] The magnitude of adaptation in the FFA was significantly less in

the dyslexia group than the control group [two-tailed independent-sample t-test, $t(38) = 3.37$, $p < 0.002$]. (A Bonferroni-corrected α of 0.0167 was adopted for significance of the ROI-based t-tests in this analysis).

4.4 Discussion

In these four additional experiments we found that adaptation of the fMRI BOLD signal, a putative index of rapid cortical plasticity, was diminished in individuals with dyslexia for every stimulus type assessed – auditory language, visual language, objects, and faces. This deficit in adaptation was found specifically in, and limited to, those brain regions known to be critically involved in processing stimuli of each domain (Hickok & Poeppel, 2007; Chandrasekaran, Chan, & Wong, 2011; Pugh *et al.*, 2008; Malach *et al.*, 1995; Weiner *et al.*, 2010). The breadth of this deficit, across brain regions and across stimulus types, suggests that a dysfunction of rapid cortical plasticity may be a fundamental physiological property of the dyslexic brain.

Individuals with dyslexia exhibited significantly diminished plasticity during the repetition of all types of linguistic stimuli. In Experiment 2, we had observed significantly reduced neural adaptation to phonetic consistency during speech perception in individuals with dyslexia relative to controls. This difference is consistent with behavioral impairments in dyslexia for learning the phonetic consistency of individual talkers (Perrachione, Del Tufo, Gabrieli, 2011) and may represent a neurophysiological source for phonological impairments in this disorder. Experiments 3a and 3b expanded on this result to reveal adaptation deficits in dyslexia that extended even to highly salient stimulus repetitions in both auditory and visual language tasks. In these latter two experiments, the dyslexia group also uniquely exhibited limited areas of significantly enhanced activation following stimulus repetitions, which may indicate underspecified long-term lexical representations in dyslexia (Pugh *et al.*, 2008; Turk-Browne *et al.*, 2007). Indeed, the regions in which the dyslexia group exhibited significantly diminished adaptation across all

three language tasks were those widely implicated in phonological processing and lexical access – left PT and posterior MTG (Hickok & Poeppel, 2007; Chandrasekaran, Chan, & Wong, 2011).

We further observed that, less expectedly, adaptation deficits in dyslexia extended to both types of nonlinguistic stimuli assessed. In Experiment 3c, individuals with dyslexia exhibited significantly reduced neural adaptation to visual objects relative to controls. Although both the task (deviant detection) and experimental manipulation (stimulus repetition) were putatively nonverbal, visual objects are nameable, and covert category naming may have played a part in this task. Rapid-naming deficits, in which individuals with dyslexia are slower than controls when producing automatized categorical responses to visual stimuli, but are unimpaired in their recognition of such stimuli, sometimes accompany phonological impairment in this disorder (Wolf, 1984). However, in Experiment 3d we observed the extension of adaptation deficits to (unfamiliar) faces – a stimulus category that is not inherently nameable, and for which no behavioral impairments have been found in dyslexia. Further, this most unexpected reduction in cortical plasticity was evident in individually defined FFA regions, which suggests that the observed plasticity deficits were not simply due to greater variation in the location of plasticity among individuals with dyslexia than individuals without dyslexia. Together, these results suggest that diminished rapid plasticity is not dependent on overt or covert linguistic processing, but instead appears to affect perceptual systems generally in dyslexia.

5. Conclusions: A neural adaptation dysfunction framework for understanding the source of phonological deficits in dyslexia

Dysfunction of rapid cortical plasticity is a compelling candidate for a core etiological deficit in dyslexia because of the critical role this mechanism plays in the types of associative learning that underlie the development of robust, abstract perceptual categories (Weinberger, 2004). Reduced ability to construct short-term representations of stimulus consistency to enhance perception necessarily precludes the development of robust, long-term representation of perceptual categories. Strong perceptual categories are crucial for coordinating the complex abstract relationships involved in reading development – namely, mapping abstract representations of the sounds of spoken language to abstract representations of the visual symbols used in written language. If the perceptual categories on either or both sides of this correspondence are in some way underspecified or not readily available, the task of accessing linguistic representations via print becomes the sort of disproportionately slower, more difficult endeavor seen in individuals with dyslexia.

Dyslexia has long been understood to be a consequence of underlying disorders of

linguistic or perceptual processing. There is a broad consensus that difficulty developing typical reading abilities results from a core deficit in phonological processing in dyslexia (Bradley & Bryant, 1983; Lyon, Shaywitz & Shaywitz, 2003, Vellutino *et al.*, 2004; Ramus & Szenkovits, 2008; Gabrieli, 2009). Concomitant low-level and non-verbal auditory perceptual deficits have often been shown to accompany reading impairments, and some have suggested that such perceptual impairments may be the source of phonological processing difficulties (Tallal & Piercy, 1973; Goswami, 2011). On the other hand, the present findings point to a dysfunction of plasticity as a core disorder from which impairments in both linguistic and non-verbal perceptual processing may arise. Ultimately, the core disorder leading to phonological impairments in dyslexia may be one of learning, not perception, although this learning deficit resides in perceptual systems.

A deficit of perceptual learning arising from dysfunctional rapid cortical plasticity is well situated to reconcile the range of other behavioral, neurophysiological, and neuroanatomical observations in dyslexia. A behavioral "anchoring deficit" has been proposed to explain why individuals with dyslexia appear to have impaired perceptual abilities for tasks involving stimulus repetition (Ahissar *et al.*, 2006; Banai & Ahissar, 2010). Correspondingly, a behavioral "noise exclusion deficit" has been proposed to explain behavioral impairment in dyslexia for tasks involving auditory or visual noise (Sperling *et al.*, 2005, 2006; Ziegler *et al.*, 2009). Given that similar rapid cortical plasticity mechanisms underlie both enhanced perceptual representation of repeated, behaviorally relevant stimuli and improved detection of stimuli in the presence of noise (Fritz *et al.*, 2003; Edeline, Pham, & Weinberger, 1993, Atiani *et al.*, 2009; Ahveninen *et al.*, 2011), both anchoring and noise exclusion deficits may plausibly result from the dysfunction of a common mechanism.

Individuals with poor reading and phonological abilities have also been shown to have reduced fidelity in their auditory brainstem response (ABR) (Hornickel *et al.*, 2009) – an evoked potential originating in inferior colliculus and measured over thousands of

repetitions of a single stimulus. Dysfunctional cortical plasticity may diminish the corticofugal modulation necessary for attaining high fidelity stimulus representation via auditory brainstem plasticity (Suga *et al.*, 2002). Typical readers, but not individuals with dyslexia, exhibit a correspondingly enhanced ABR in the presence of stimulus consistency (Chandrasekaran *et al.*, 2009). Moreover, the amount of ABR enhancement by stimulus consistency is correlated with behavioral measures of noise-exclusion, further demonstrating that dysfunction of a single mechanism could underlie both anchoring (adaptation) and noise exclusion.

A number of important questions remain given limitations of the data presented here. First, Experiments 2 and 3 were designed to maximize our ability to detect fMRI adaptation, but this came at the cost of detecting behavioral enhancement following stimulus repetition as in, for example, classical repetition priming paradigms. The correspondence between simultaneous deficits in fMRI BOLD signal adaptation and perceptual adaptation-related behavioral deficits in dyslexia remains to be further explored. Second, the current studies included only adult participants, and future research with young struggling readers and pre-readers at familial risk of developmental dyslexia is necessary for elaborating a causal relationship between neural adaptation deficits and the phonological deficits preceding reading difficulties.

Third, the specific mechanism causing reduced neural adaptation in dyslexia remains to be delineated. Stimuli in all of the Adaptation conditions were both highly repetitive and highly predictable, such that these experiments could not discriminate between top-down expectation-driven and bottom-up percept-driven processes. A ready alternative explanation for the observed differences in neural adaptation between the control and dyslexia groups may be that individuals with dyslexia are less able to differentially engage attention between perceptually demanding tasks (here, deviant target detection during the no-adaptation conditions) and comparatively less-demanding ones (deviant detection during the adaptation condition). By maintaining a consistently high

(or low) attentive state, top-down influences may not have differentially affected perceptual processing in sensory cortex in the dyslexia group, whereas differential deployment of attention between the two conditions may account for the adaptation effects observed in controls. There are two reasons to disprefer such a hypothesis: First, there is no evidence from any of the five stimulus types for between-group differences in activation in fronto-parietal cortical areas known to direct the engagement of attention (Kastner & Ungerleider, 2000; Hopfinger, Buonocore, & Mangun, 2000). Second, significant adaptation differences were originally observed in the speech perception task of Experiment 2, in which the attentional demands of the high- and low-variability conditions presumably did not differ in the same way the did for the tasks in Experiment 3.

However, the role of top-down processes in shaping perception are not to be completely discounted, as they play a major role in shaping perceptual processes. In humans, perceptual expectation strongly influences the magnitude of neural adaptation (Summerfield *et al.*, 2008, 2011; Alink *et al.*, 2010; Costa-Faidella *et al.*, 2011; Todorovic *et al.*, 2011). Animal models have shown that rapid cortical plasticity following stimulus repetition requires feedback from higher-order cortices signaling behavioral engagement with the stimuli (Fritz *et al.*, 2003; Polley, Steinberg, & Merzenich, 2011; Ahveninen *et al.*, 2011; Froemke, Merzenich, & Schreiner, 2007). The neural adaptation deficits observed in individuals with dyslexia might represent a failure to generate robust perceptual expectations: Higher cortical areas may fail to establish the necessary feedback signals to sensory cortices for inducing plasticity. Alternatively, the reduced plasticity may result from an altered interaction between top-down expectation and bottom-up perceptual processes via differences in local neuromodulatory connections. Adaptation-related plasticity depends on finely tuned neuromodulatory input (Weinberger, 2004; Froemke, Merzenich, & Schreiner, 2007) and is related to lamina-specific synchronization in sensory cortex (Hansen & Dragoi, 2011). In dyslexia, there is some evidence for the existence of microanatomical abnormalities that disrupt laminar structure (Galaburda *et al.*, 2006), which may interfere with the local or long-range network connectivity sup-

porting adaptation-related plasticity. In particular, there is an extensive literature in animal models demonstrating the necessity of basal forebrain cholinergic input for rapid cortical plasticity (*e.g.*, Froemke, Merzenich, & Schreiner, 2007), as well as a corresponding literature in humans demonstrating cholinergic modulation of perceptual learning and neural adaptation (Furey, Pietrini, & Haxby, 2000; Thiel *et al.*, 2001, 2002; Dinse *et al.*, 2003; Rokem & Silver, 2010). Further studies that investigate the role of top-down expectation and neuromodulatory effects (including particularly the role of acetylcholine) may clarify the basis for exiguous neural adaptation in dyslexia, as well as relate these findings to possible attentional mechanisms that support such plasticity.

Learning to read depends on the ability to orchestrate, across perceptual modalities, the complex correspondence between abstract phonological representations of speech sounds and abstract orthographic representations of written symbols – a task that becomes disproportionately more difficult if either or both sets of perceptual representations are impaired. Successful development of the robust perceptual representations underlying phonological and orthographic categories depends on a cascade of neural plasticity beginning with mechanisms for rapidly constructing representations of short-term consistency in behaviorally-relevant stimuli. In these experiments, we have shown that such rapid cortical plasticity is diminished in dyslexia – independent of perceptual modality or linguistic content. A generalized dysfunction of rapid cortical plasticity provides a plausible mechanistic basis for the phonological and reading deficits in dyslexia, as well as a framework for reconciling the wide range of other behavioral and neural differences observed in this disorder, including impairments in rapid naming, noise exclusion, and anchoring/adaptation.

References

Adab, H.Z., & Vogels, R. (2011). "Practicing coarse orientation discrimination improves orientation signals in macaque cortical area V4." *Current Biology*, 21, 1661-1666.

Adams, M.J. (1994). *Beginning to Read: Thinking and Learning about Print.* MIT Press, Cambridge, MA.

Ahissar, M., Protopapas, A., Reid, M., & Merzenich, M.M. (2000). "Auditory processing parallels reading abilities in adults." *Proceedings of the National Academy of Sciences: USA,* 97, 6832–6837.

Ahissar, M., Lubin, Y., Putter-Katz, H. & Banai, K. (2006). "Dyslexia and the failure to form a perceptual anchor." *Nature Neuroscience*, 9, 1558-1564.

Ahveninen, J., Hämäläinen, M., Jääskeläinen, I.P., Ahlfors, S.P., Huang, S., Lin, F., Raij, T., Sams, M., Vasios, C.E., Belliveau, J.W. (2011). "Attention-driven auditory cortex short-term plasticity helps segregate relevant sounds from noise." *Proceedings of the National Academy of Sciences: USA*, 108, 4182-4187.

Alain, C., Snyder, J.S., He, Y., Reinke, K.S. (2007). "Changes in auditory cortex parallel rapid perceptual learning." *Cerebral Cortex*, 17, 1074-1084.

Alink, A., Schwiedrzik, C.M., Kohler, A., Singer, W., & Muckli, L. (2010). "Stimulus predictability reduces responses in primary visual cortex." *Journal of Neuroscience*, 30, 2960-2966.

Allen, J.S. & Miller, J.L. (2004). "Listener sensitivity to individual talker differences in voice-onset-time." *Journal of the Acoustical Society of America*, 115, 3171-3183.

Atiani, S., Elhilali, M., David, S.V., Fritz, J.B., Shamma, S.A. (2009). "Task difficulty and performance induce diverse adaptive patterns in gain and shape of primary auditory cortical receptive fields." *Neuron*, 61, 467-480.

Avants, B.B., Epstein, C.L., Grossman, M., Gee, J.C. (2008). "Symmetric diffeomorphic image registration with cross-correlation: Evaluating automated labeling of elderly and neurodegenerative brain." *Medical Image Analysis*, 12, 26-41.

Badian, N.A. (1993). "Phonemic awareness, naming, visual symbol processing, and reading." *Reading and Writing,* 5, 87-100.

Bahrick, H.P., Bahrick, P.O., and Wittlinger, R.P. (1975). "Fifty years of memory for names and faces: a cross-sectional approach." *Journal of Experimental Psychology: General* 104, 54-75.

Banai, K., Ahissar, M. (2010). "On the importance of anchoring and the consequences of its impairment in dyslexia." *Dyslexia*, 16, 240-257.

Barcroft, J. & Sommers, M. S. (2005). "Effects of acoustic variability on second language vocabulary learning," *Studies in Second Language Acquisition*, 27, 387-414.

Belin, P., Zatorre, .R.J., Hoge, R., Evans, A.C., & Pike, P. (1999). "Event-related fMRI of the auditory cortex." *NeuroImage*, 10, 417-429.

Belin, P. & Zatorre, R.J. (2003). "Adaptation to speaker's voice in right anterior temporal lobe." *NeuroReport*, 14, 2105-2109.

Belin, P., Fecteau, S.,& Bédard, C. (2004). "Thinking the voice: Neural correlates of voice perception." *Trends in Cognitive Sciences*, 3, 129–135.

Bell, A.H., Malecek, N.J., Morin, E.L., Hadj-Bouziane, F., Tootell, R.B.H., Ungerleider, L.G. (2011). "Relationship between functional magnetic resonance imaging-identified regions and neuronal category selectivity." *Journal of Neuroscience*, 31, 12229-12240.

Blau, V., van Atteveldt, N., Ekkebus, M., Goebel, R., Blomert, L. (2009). "Reduced neural integration of letters and speech sounds links phonological and reading deficits in adult dyslexia." *Current Biology*, 19, 503-508.

Blomert, L., Mitterer, H., & Paffen, C. (2004). "In search of the auditory, phonetic, and/or phonological problems in dyslexia: Context effects in speech perception." *Journal of Speech, Language and Hearing Research*, 47, 1030-1047.

Boersma, P. (2001). "Praat, a system for doing phonetics by computer." *Glot International*, 5, 341-345.

Brachacki, G.W.Z., Fawcett, A.J., and Nicolson, R.I. (1994). "Adults with dyslexia have a deficit in voice recognition." *Perceptual Motor Skills,* 78, 304-306.

Bradley, L., and Bryant, P.E. (1983). "Categorizing sounds and learning to read - a causal connection." *Nature*, 301, 419-421.

Bradlow, A.R., Nygaard, L.C., & Pisoni, D.B. (1999). "Effects of talker, rate, and amplitude variation on recognition memory for spoken words." *Perception and Psychophysics*, 61, 206-219.

Bruck, M. (1992). "Persistence of dyslexics' phonological awareness deficits." *Developmental Psychology*, 28, 874-886.

Bryant, P.E., MacLean, M., Bradley, L.L., & Crossland, J. (1990). "Rhyme and alliteration, phoneme detection and learning to read." *Developmental Psychology*, 26, 429-438.

Buckner, R.L., Andrews-Hanna, J.R., & Schacter, D.L. (2008). "The brain's default network: Anatomy, function, and relevance to disease." *Annals of the New York Academy of Sciences*, 1124, 1-38.

Chait, M., Eden, G., Poeppel, D., Simon, J.Z., Hill, D.F., Flowers, D.L. (2007). "Delayed detection of tonal targets in background noise in dyslexia." *Brain and Language*, 102, 80-90.

Chandrasekaran, B., Hornickel, J., Skoe, E., Nicol, T., & Kraus, N. (2009). "Context-dependent encoding in the human auditory brainstem relates to hearing speech in noise: implications for developmental dyslexia." *Neuron*, 64, 311-319.

Chandrasekaran, B., Chan, A.H.D., Wong, P.C.M. (2011). "Neural processing of what and who information in speech." *Journal of Cognitive Neuroscience*, 23, 2690-2700.

Cheung, H., Chung, K.K.H., Wong, S.W.L., McBridge-Chang, C., Penney, T.B., & Ho, C.S.H. (2009). "Perception of tone and aspiration contrasts in Chinese children with dyslexia." *Journal of Child Psychology and Psychiatry*, 50, 726-733.

Clopper, C. G. & Pisoni, D. B. (2004). "Effects of talker variability on perceptual learning of dialects," *Language and Speech*, 47, 207-239.

Costa-Faidella, J., Baldweg, T., Grimm, S., & Escera, C. (2011). "Interactions between 'what' and 'when' in the auditory system: Temporal predictability enhances repetition suppression." *Journal of Neuroscience*, 31, 18590-18597.

Creel, S.C., Aslin, R.N., & Tanenhaus, M.K. (2008). "Heeding the voice of experience: The role of talker variation in lexical access." *Cognition*, 106, 633-664.

Dale, A.M., Fischl, B., & Sereno, M.I., (1999). "Cortical surface-based analysis. I. Segmentation and surface reconstruction." *NeuroImage*, 9, 179-194.

Denckla, M.B. & Rudel, R.G. (1976). "Rapid 'automatized' naming (R.A.N.): Dyslexia differentiated from other learning disabilities." *Neuropsychologia*, 14, 471-479.

Dinse, H.R., Ragert, P., Pleger, B., Schwenkreis, P., Tegenthoff, M. (2003). "Pharmacological modulation of perceptual learning and associated cortical reorganization. *Science*, 301, 91-94.

Edeline, J.-M., Pham, P., & Weinberger, N.M. (1993). "Rapid development of learning-induced receptive field plasticity in the auditory cortex." *Behavioral Neuroscience*, 107, 539-551.

Eden, G.F., VanMeter, J.W., Rumsey, J.M., Maisog, J.M., Woods, R.P., & Zeffiro, T.A. (1996). "Abnormal processing of visual motion in dyslexia revealed by functional

brain imaging." *Nature*, 382, 66-69.

Fioravante, D., Regehr, W.G. (2011). "Short-term forms of presynaptic plasticity." *Current Opinion in Neurobiology*, 21, 269-274.

Flege, J.E. (1995). "Two procedures for training a novel second language phonetic contrast," *Applied Psycholinguistics*, 16, 425-442.

Franceschini, S., Gori, S., Ruffino, M., Pedrolli, K., & Facoetti, A. (2012). "A causal link between visual spatial attention and reading acquisition." *Current Biology*, 22, 814-819.

Friston, K.J., Fletcher, P., Josephs, O., Holmes, A., Rugg, M.D., & Turner, R. (1998). "Event-related fMRI: Characterizing differential responses." *NeuroImage*, 7, 30-40.

Fritz, J., Shamma, S., Elhilali, M., Klein, D. (2003). "Rapid task-related plasticity of spectrotemporal receptive fields in primary auditory cortex." *Nature Neuroscience*, 6, 1216-1223.

Froemke, R.C., Merzenich, M.M., Schreiner, C.E. (2007). "A synaptic memory trace for cortical receptive field plasticity." *Nature*, 450, 425-429.

Furey, M.L., Pietrini, P., & Haxby, J.V. (2000). "Cholinergic enhancement and increased selectivity of perceptual processing during working memory." *Science*, 290, 2315-2319.

Gaab, N., Gabrieli, J.D.E., & Glover, G.H. (2007). "Assessing the influence of scanner background noise on auditory processing. I. An fMRI study comparing three experimental designs with varying degrees of scanner noise." *Human Brain Mapping*, 28, 703-720.

Gabrieli, J.D.E. (2009). "Dyslexia: a new synergy between education and cognitive neuroscience." *Science* 325, 280-283.

Galaburda, A.M., LoTurco, J., Ramus, F., Fitch, R.H., & Rosen, G.D. (2006). "From genes to behavior in developmental dyslexia." *Nature Neuroscience*, 9, 1213-1217.

Galaburda, A.M., Menard, M.T., & Rosen, G.D. (1994). "Evidence for aberrant auditory anatomy in developmental dyslexia." *Proceedings of the National Academy of Sciences: USA*, 91, 8010-8013.

Galindo-Leon, E.E., Lin, F.G., Liu, R.C. (2009). "Inhibitory plasticity in a lateral band improves cortical detection of natural vocalizations." *Neuron*, 62, 705-716.

Garrido, M.I., Kilner, J.M., Kiebel, S.J., Stephan, K.E., Baldeweg, T., Friston, K.J. (2009). "Repetition suppression and plasticity in the human brain." *NeuroImage*, 48, 269-279.

Ghosh, S.S., Kovelman, I., Lymberis, J., Gabrieli, J.D. (2009) "Incorporating hemodynamic response functions to improve analysis models for sparse-acquisition experiments." *NeuroImage*, 47, *Organization for Human Brain Mapping 2009 Annual*

Meeting.

Goggin, J.P., Thompson, C.P., Strube, G., and Simental, L.R. (1991). "The role of language familiarity in voice identification." *Memory & Cognition* 19, 448-458.

Goldinger, S.D. (1998). "Echoes of echoes? An episodic theory of lexical access." *Psychological Review*, 105, 251-279.

Goldinger, S.D. (2007). "A complementary-systems approach to abstract and episodic speech perception." *Proceedings of the 16th Meeting of the International Congress of Phonetic Sciences*,(Saarbrücken, Germany).

Gorgolewski, K., Burns, C.D., Madison, C., Clark, D., Halchenko, Y.O., Waskom, M.L. & Ghosh, S.S. (2011). "Nipype: A flexible, lightweight and extensible neuroimaging data processing framework." *Frontiers in Neuroinformatics*, 5, doi:10.3389/fninf.2011.00013.

Goswami, U. (2011). "A temporal sampling framework for developmental dyslexia." *Trends in Cognitive Sciences*, 15, 3-10.

Green, K.P., Tomiak, G.R., & Kuhl, P.K. (1997) ." The encoding of rate and talker information during phonetic perception." *Perception and Psychophysics*, 59, 675-692.

Grill-Spector, K., & Malach, R. (2001). "fMRI adaptation: A tool for studying the functional properties of human cortical neurons." *Acta Psychologica*, 107, 293-321.

Grosenick, L., Clement, T.S., and Fernald, R.D. (2007). "Fish can infer social rank by observation alone." *Nature* 446, 102-102.

Grossberg, S. (1980). "How does a brain build a cognitive code?" *Psychological Review*, 87, 1-51.

Hailstone, J.C., Crutch, S.J., Vestergaard, M.D., Patterson, R.D., and Warren, J.D. (2010). "Progressive associative phonagnosia: A neuropsychological analysis." *Neuropsychologia* 48, 1104-1114.

Hall, D.A., Haggard, M.P., Akeroyd, M.A., Palmer, A.R., Summerfield, A.Q., Elliot, M.R., Gurney, E.M., & Bowtell, R.W. (1999). "'Sparse' temporal sampling in auditory fMRI." *Human Brain Mapping*, 7, 213-223.

Hansen, B.J. & Dragoi, V. (2011). "Adaptation-induced synchronization in laminar cortical circuits." *Proceedings of the National Academy of Sciences: USA*, 108, 10720-10725.

Hazan, V., Messaoud-Galusi, S., Rosen, S., Nouwens, S., & Shakespeare, B. (2009). "Speech perception abilities of adults with dyslexia: Is there any evidence for a true deficit?" *Journal of Speech, Language, and Hearing Research*, 52, 1510-1529.

Hecaen H. & Angelergues, R. (1962). "Agnosia for faces (prosopagnosia)." *Archives of Neurology,* 7, 92+.

Hickok, G., Poeppel, D. (2007). "The cortical organization of speech processing." *Nature Reviews Neuroscience*, 8, 393-402.

Hopfinger, J.B., Buonocore, M.H., & Mangun, G.R. (2000). "The neural mechanisms of top-down attention." *Nature Neuroscience*, 3, 284-291.

Hornickel, J. Skoe, E., Nicol, T., Zecker, S., Kraus, N. (2009). "Subcortical differentiation of stop consonants relates to reading and speech-in-noise perception." *Proceedings of the National Academy of Sciences: USA*, 106, 13022-13027.

Insley, S.J. (2000). "Long-term vocal recognition in the northern fur seal." *Nature* 406, 404-405.

Institute of Electrical and Electronics Engineers (1969). "IEEE recommended practices for speech quality measurements." *IEEE Transactions on Audio and Electroacoustics,* 17, 225-246.

Jääskeläinen, I.P., Ahveninen, J., Belliveau, J.W., Raij, T., & Sams, M. (2007). "Short-term plasticity in auditory cognition." *Trends in Neurosciences*, 30, 653-661.

Janik, V.M., Sayigh, L.S., and Wells, R.S. (2006). "Signature whistle shape conveys identity information to bottlenose dolphins." *Proceedings of the National Academy of Sciences: USA*, 103, 8293-8297.

Jouventin, P., Aubin, T., and Lengagne, T. (1999). "Finding a parent in a king penguin colony: the acoustic system of individual recognition." *Animal Behavior,* 57, 1175-1183.

Kaganovich, N., Francis, A.L., and Melara, R.D. (2006). "Electrophysiological evidence for early interaction between talker and linguistic information during speech perception." *Brain Research* 1114, 161-172.

Kanwisher, N., McDermott, J., & Chun, M.M. (1997). "The fusiform face area: A module in human extrastriate cortex specialized for face perception." *Journal of Neuroscience*, 17, 4302-4311.

Kanwisher, N. & Yovel, G. (2006). "The fusiform face area: a cortical region specialized for the perception of faces." *Philosophical Transactions of the Royal Society B – Biological Sciences*, 361, 2109-2128.

Karavanich, C., and Atema, J. (1998). "Individual recognition and memory in lobster dominance." *Animal Behavior*, 56, 1553-1560.

Kastner, S. & Ungerleider, L.G. (2000). "Mechanisms of visual attention in the human cortex." *Annual Review of Neuroscience*, 23, 315-341.

Kazial, K.A., Kenny, T.L., & Burnett, S.C. (2008). "Little brown bats (Myotis lucifugus) recognize individual identity of conspecifics using sonar calls." *Ethology*, 114, 469-478.

Kingston, J. (2003). "Learning foreign vowels," *Language and Speech*, 46, 295-349.

Klein, A., Andersson, J., Ardekani, B.A., Ashburner, J., Avants, B., Chiang, M.-C., Christensen, G.E., Collins, D.L., Gee, J., Hellier, P., Song, J.H., Jenkinson, M., Lepage, C., Rueckert, D., Thompson, P., Vercauteren, T., Woods, R.P., Mann, J.J., Parsey, R.V. (2009). "Evaluation of 14 nonlinear deformation algorithms applied to human brain MRI registration." *NeuroImage*, 46, 786-802.

Klein, A., Ghosh, S.S., , Avants, B., Yeo, B.T.T. Fischl, B. Ardekani, B., Gee., J.C., Mann, J.J., Parsey, R.V. (2010). "Evaluation of volume-based and surface-based brain image registration methods." *NeuroImage*, 51, 214-220.

Knösche, T.R., Lattner, S., Maess, B., Schauer, M., and Friederici, A.D. (2002). "Early parallel processing of auditory word and voice information." *NeuroImage* 17, 1493-1503.

Krekelberg, B., Boynton, G.M., van Wezel, R.J.A. (2006). "Adaptation: from single cells to BOLD signals." *Trends in Neurosciences*, 29, 250-256.

Kuhl, P.K. (2004). "Early language acquisition: Cracking the speech code." *Nature Reviews Neuroscience*, 5, 831-843.

Lee, C., Middlebrooks, J.C. (2011). "Auditory cortex spatial sensitivity sharpens during task performance." *Nature Neuroscience*, 14, 108-114.

Lengagne, T., Aubin, T., Jouventin, P., and Lauga, J. (2000). "Perceptual salience of individually distinctive features in the calls of adult king penguins." *Journal of the Acoustical Society of America,* 107, 508-516.

Levi, S.V., Winters, S.J. & Pisoni, D.B. (2011). "Effects of cross-language voice training on speech perception: Whose familiar voices are more intelligible?" *Journal of the Acoustical Society of America,* 130, 4053-4062.

Lively, S.E., Logan, J. S., & Pisoni, D. B. (1993). "Training Japanese listeners to identify English /r/ and /l/. II: The role of phonetic environment and talker variability in learning new perceptual categories," *Journal of the Acoustical Society of America,* 94, 1242-1255.

Livingstone, M.S., Rosen, G.D., Drislane, F.W., & Galaburda, A.M. (1991). "Physiological and anatomical evidence for a magnocellular defect in developmental dyslexia." *Proceedings of the National Academy of Sciences: USA*, 88, 7943-7947.

Lyon, G.R., Shaywitz, S.E., Shaywitz, B.A. (2003). "A definition of dyslexia." *Annals of Dyslexia*, 53, 1-14.

Malach, R., Reppas, J.B., Benson, R.R., Kwong, K.K., Jiang, H., Kennedy, W.A., Ledden, P.J., Brady, T.J., Rosen, B.R., Tootell, R.B. (1995). "Object-related activity revealed by functional magnetic resonance imaging in human occipital cortex." *Proceedings of the National Academy of Sciences: USA*, 92, 8135– 8139.

Manis, F.R., McBride-Chang, C., Seidenberg, S., Keating, P., Doi, L.M., Munson, B., & Pe-

tersen, A. (1997). "Are speech perception deficits associated with developmental dyslexia?" *Journal of Experimental Child Psychology*, 66, 211-235.

Martin, J. & Lovegrove, W. (1987). "Flicker contrast sensitivity in normal and specifically-disabled readers." *Perception*, 16, 215-221.

Melby-Lervåg, M., Lyster, S.-A.H., & Hulme, C. (2012). "Phonological skills and their role in learning to read: A meta-analytic review." *Psychological Bulletin*, 138, 322-352.

Messaoud-Galusi, S., Hazan, V., & Rosen, S. (2011). "Investigating speech perception in children with dyslexia: Is there evidence of a consistent deficit in individuals?" *Journal of Speech, Language and Hearing Research*, 54, 1682-1701.

Moores, E., Cassim, R., & Talcott, J.B. (2011). "Adults with dyslexia exhibit large effects of crowding, increased dependence on cues, and detrimental effects of distractors in visual search tasks." *Neuropsychologia*, 49, 3881-3890.

Mozzachiodi, R. & Byrne, J.H. (2010). "More than synaptic plasticity: Role of nonsynaptic plasticity in learning and memory." *Trends in Neurosciences*, 33, 17-26.

Mullennix, J.W. & Pisoni, D.B. (1990). "Stimulus variability and processing dependencies in speech perception." *Perception and Psychophysics*, 47, 379-390.

Nagarajan, S., Mahncke, H., Salz, T., Tallal, P., Roberts, T., Merzenich, M. (1999). "Cortical auditory signal processing in poor readers." *Proceedings of the National Academy of Sciences: USA*, 96, 6483-6488.

Newman, R.S. & Evers, S. (2007). "The effect of talker familiarity on stream segregation." *Journal of Phonetics*, 35, 85-103.

Nygaard, L.C., Sommers, M.S., & Pisoni, D.B. (1994). "Speech perception as a talker-contingent process." *Psychological Science*, 5, 42-46.

Nygaard, L.C. & Pisoni, D.B. (1998). "Talker-specific learning in speech perception." *Perception and Psychophysics*, 60, 355-376.

Open Speech Repository. (2005). *Open Speech Repository*. http://www.voiptroubleshooter.com/openspeech/index.html

Palmeri, T.J., Goldinger, S.D., & Pisoni, D.B. (1993). "Episodic encoding of voice attributes and recognition memory for spoken words." *Journal of Experimental Psychology – Learning, Memory, and Cognition*, 19, 309-328.

Perrachione, T.K., and Wong, P.C.M. (2007). "Learning to recognize speakers of a non-native language: Implications for the functional organization of human auditory cortex." *Neuropsychologia,* 45, 1899-1910.

Perrachione, T.K., Pierrehumbert, J.B., and Wong, P.C.M. (2009). "Differential neural contributions to native- and foreign-language talker identification." *Journal of Experimental Psychology – Human Perception and Performance,* 35, 1950-1960.

Perrachione, T.K., Chiao, J.Y., and Wong, P.C.M. (2010). "Asymmetric cultural effects on perceptual expertise underlie an own-race bias for voices." *Cognition* 114, 42-55.

Perrachione, T.K., Del Tufo, S.N., Gabrieli, J.D.E. (2011). "Human voice recognition depends on language ability." *Science*, 333, 595.

Perrachione, T.K., Gabrieli, J.D.E., Ghosh, S.S. (2011). "Optimized design and analysis of sparse-sampling functional magnetic resonance imaging experiments of speech and hearing.", *161st Meeting of the Acoustical Society of America*, (Seattle).

Perrachione, T.K., Del Tufo, S.N., Ghosh, S.S., Gabrieli, J.D.E. (2011). "Phonetic variability in speech perception and the phonological deficit in dyslexia." *Proceedings of the 17th Meeting of the International Congress of Phonetic Sciences*, (Hong Kong).

Peterson, G.E. & Barney, H.L. (1952). "Control methods used in a study of the vowels." *Journal of the Acoustical Society of America*, 24, 175-184.

Polka, L., Colantonio, C., & Sundara, M. (2001). "A cross-language comparison of /d/-/ð/ perception: Evidence for a new developmental pattern." *Journal of the Acoustical Society of America*, 109, 2190-2201.

Polley, D.B., Steinberg, E.E., & Merzenich, M.M. (2011). "Perceptual learning directs auditory cortical map reorganization through top-down influences." *Journal of Neuroscience*, 26, 4970-4982.

Proops, L., McComb, K., and Reby, D. (2009). "Cross-modal individual recognition in domestic horses (Equus caballus)." *Proceedings of the National Academy of Sciences: USA,* 106, 947-951.

Pufpaff, L.A. (2009). "A developmental continuum of phonological sensitivity scales." *Psychology in the Schools*, 46, 679-691.

Pugh, K., Frost, S.J., Sandak, R., Landi, N., Rueckl, J.G., Constable, R.T., Seidenberg, M.S., Fulbright, R.K., Katz, L., & Mencl, W.E. (2008). "Effects of stimulus difficulty and repetition on printed word identification: An fMRI comparison of nonimpaired and reading-disabled adolescent cohorts." *Journal of Cognitive Neuroscience,* 20, 1146-1160.

Ramus, F. & Szenkovits, G. (2008). "What phonological deficit?" *Quarterly Journal of Experimental Psychology*, 61. 129-141.

Recanzone, G.H., Schreiner C.E., Merzenich, M.M. (1993). "Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys." *Journal of Neuroscience*, 13, 87-103.

Reed, A., Riley, J., Carraway, R., Carrasco, A., Perez, C., Jakkamsetti, V., Kilgard, M.P. (2011). "Cortical map plasticity improves learning but is not necessary for improved performance." *Neuron*, 70, 121-131.

Rokem, A., & Silver, M.A. (2010). "Cholinergic enhancement augments magnitude and

specificity of visual perceptual learning in healthy humans." *Current Biology*, 20, 1723-1728.

Rosen, S. (2003). "Auditory processing in dyslexia and specific language impairment: Is there a deficit? What is it's nature? Does it explain anything?" *Journal of Phonetics*, 31, 509-527.

Rüsseler J, Johannes S, Münte TF. (2003). "Recognition memory for unfamiliar faces does not differ for adult normal and dyslexic readers: An event-related brain potential study." *Clinical Neurophysiology*, 114, 1285-1291.

Rutkowski, R.G., Weinberger, N.M. (2005). "Encoding of learned importance of sound by magnitude of representational area in primary auditory cortex." *Proceedings of the National Academy of Sciences: USA*, 102, 13664-13669.

Serniclaes, W., Sprenger-Charolles, L., Carré, R., Demonet, J.-F. (2001). "Perceptual discrimination of speech sounds in developmental dyslexia." *Journal of Speech, Language, and Hearing Research*, 44, 384-399.

Serniclaes, W., van Heghe, S., Mousty, P., Carre, R., & Sprenger-Charolles, L. (2004). "Allophonic mode of speech perception in dyslexia." *Journal of Experimental Child Psychology*, 87, 336–361.

Shankweiler, D., Crain, S., Katz, L., Fowler, A.E., Liberman, A.M., Brady, S.A., Thornton, R., Lundquist, E., Dreyer, L., Fletcher, J.M., Stuebing, K.K., Shaywitz, S.E., & Shaywitz, B.A. (1995). "Cognitive profiles of reading-disabled children: Comparison of language skills in phonology, morphology, and syntax." *Psychological Science*, 6, 149–156.

Shaywitz, S.E. & Shaywitz, B.A. (2005). "Dyslexia (specific reading disability)." *Biological Psychiatry*, 57, 1301-1309.

Sjerps, M.J., Mitterer, H., & McQueen, J.M. (2011). "Listening to different speakers: On the time-course of perceptual compensation for vocal-tract characteristics." *Neuropsychologia*, 49, 3831-3846.

Smith-Spark, J. & Moore, V. (2009). "The representation and processing of familiar faces in dyslexia: differences in age of acquisition effects." *Dyslexia*, 15, 129-146.

Snodgrass, J.G., Vanderwart, M. (1980). "Standardized set of 260 pictures: Norms for name agreement, image agreement, familiarity, and visual complexity." *Journal of Experimental Psychology-Human Learning and Memory*, 6, 174-215.

Snowling, M., van Wagtendonk, B., & Stafford , C. (1988). "Object-naming deficits in developmental dyslexia." *Journal of Research in Reading*, 11, 67-85.

Snowling, M. (1998). "Dyslexia as a phonological deficit: Evidence and implications." *Child and Adolescent Mental Health*, 3, 4-11.

Sperling, A.J., Lu, Z., Manis, F.R., Seidenberg, M.S. (2005). "Deficits in perceptual noise

exclusion in developmental dyslexia." *Nature Neuroscience*, 8, 862-863.

Sperling, A.J., Lu, Z., Manis, F.R., Seidenberg, M.S. (2006). "Motion-perception deficits and reading impairment: it's the noise, not the motion." *Psychological Science*, 17, 1047-1053.

Stein, J. & Walsh, V. (1997). "To see but not to read; The magnocellular theory of dyslexia." *Trends in Neurosciences*, 20, 147-152.

Suga, N., Xiao, Z., Ma, X., Ji, W. (2002). "Plasticity and corticofugal modulation for hearing in adult animals." *Neuron*, 36, 9-18.

Summerfield, C., Trittschuh, E.H., Monti, J.M., Mesulam, M.-M., & Egner, T. (2008). "Neural repetition suppression reflects fulfilled perceptual expectations." *Nature Neuroscience*, 11, 1004-1006.

Summerfield, C., Wyart, V., Johnen, V.M., & de Gardell, V. (2011). "Human scale electroencephalography reveals that repetition suppression varies with expectation." *Frontiers in Human Neuroscience*, 5, doi:10.3389/fnhum.2011.00067

Tallal, P. & Piercy, M. (1973). "Defects of non-verbal auditory perception in children with developmental aphasia." *Nature*, 241, 468-469.

Tanaka, H., Black, J.M., Hulme, C., Stanley, L.M., Kesler, S.R., Whitfield-Gabrieli, S., Reiss, A.L., Gabrieli, J.D.E., Hoeft, F. (2011). "The brain basis of the phonological deficit in dyslexia is independent of IQ." *Psychological Science*, 22, 1442-1451.

Theodore, R.M. & Miller, J.L. (2010). "Characteristics of listener sensitivity to talker-specific phonetic detail." *Journal of the Acoustical Society of America*, 128, 2090-2099.

Thiel, C.M., Henson, R.N.A., Morris, J.S., Friston, K.J., & Dolan, R.J. (2001). "Pharmacological modulation of behavioral and neuronal correlates of repetition priming." *Journal of Neuroscience*, 21, 6846-6852.

Thiel, C.M., Friston, K.J., & Dolan, R.J. (2002). "Cholinergic modulation of experience-dependent plasticity in human auditory cortex." *Neuron*, 35, 567-574.

Thompson, C.P. (1987). "A language effect in voice identification." *Applied Cognitive Psychology*, 1, 121-131.

Todorovic, A., van Ede, F., Maris, E. & de Lange, F.P. (2011). "Prior expectation mediates neural adaptation to repeated sounds in the auditory cortex: An MEG study." *Journal of Neuroscience*, 31, 9118-9123.

Torgesen, J. K., Wagner, R., & Rashotte, C. (1999). *Test of Word Reading Efficiency (TOWRE)*. Austin, TX: Pro-Ed.

Turk-Browne, N.B., Yi, D.-J., Leber, A.B., & Chun, M.M. (2007). "Visual quality determines the direction of neural repetition effects." *Cerebral Cortex*, 17, 425-433.

Vaessen, A., Gerretsen, P.. & Bomert, L. (2009). "Naming problems do not reflect a sec-

ond core deficit in dyslexia: Double deficits explored." *Journal of Experimental Child Psychology*, 103, 202-221.

Van Lancker, D.R. & Canter, G.J. (1982). "Impairment of voice and face recognition in patients with hemispheric damage." *Brain and Cognition*, 1, 185-195.

Van Lancker, D. & Krieman, J. (1987). "Voice discrimination and recognition are separate abilities." *Neuropsychologia*, 25, 829-834.

Vandermosten, M., Boets, B., Luts, H., Poelmans, H., Golestani, N., Wouters, J., Ghesquiere, P. (2010). "Adults with dyslexia are impaired in categorizing speech and nonspeech sound on the basis of temporal cues." *Proceedings of the National Academy of Sciences: USA,* 107, 10389-10394.

Vellutino, F.R., Fletcher, J.M., Snowling, M.J., and Scanlon, D.M. (2004). "Specific reading disability (dyslexia): what have we learned in the past four decades?" *Journal of Child Psychology and Psychiatry* 45, 2-40.

Vidyasagar, T.R. & Pammer, K. (2009). "Dyslexia: a deficit in visuo-spatial attention, not in phonological processing." *Trends in Cognitive Sciences*, 14, 57-63.

Wagner, R., & Torgesen, J. (1987). "The nature of phonological processing and its causal role in the acquisition of reading skills." *Psychological Bulletin*, 101, 192-212.

Wagner, R., Torgesen, J.K., & Rashotte, C. (1999). *Comprehensive Test of Phonological Processing (CTOPP)*. Austin, TX: Pro-Ed.

Wang, Y., Spence, M.M., Jongman, A., & Sereno, J.A. (1999). "Training American listeners to perceive Mandarin tones," *Journal of the Acoustical Society of America,* 106, 3649-3658.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI)*. San Antonio, TX: The Psychological Corporation.

Wechsler, D. (2008). *The Wechsler Adult Intelligence* Scale IV (WAIS-IV). San Antonio, TX: The Psychological Corporation.

Weinberger, N.M. (2004). "Experience-dependent response plasticity in the auditory cortex: Issues, characteristics, mechansisms, and functions." In *Plasticity of the Auditory System*, T.N. Parks, E.W. Rubel, R.R. Fay, and A.N. Popper, Eds. New York; Springer.

Weiner, K.S., Sayres, R., Vinberg, J., Grill-Spector, K. (2010). "fMRI-Adaptation and category selectivity in human ventral temporal cortex: regional differences across time scales." *Journal of Neurophysiology*, 103, 3349-3365.

Werker, J.F. & Tees, R.C. (1984). "Cross-language speech perception: Evidence for perceptual reorganization in the first year of life." *Infant Behavior and Development*, 7, 49-63.

Werker, J.F., and Tees, R.C. (2005). "Speech perception as a window for understanding

plasticity and commitment in language systems of the brain." *Devopmental Psychobiology,* 46, 233-251.

Winters, S.J., Levi, S.V., & Pisoni, D.B. (2008). "Identification and discrimination of bilingual talkers across languages." *Journal of the Acoustical Society of America*, 123, 4524-4538.

Wolf, M. (1984). "Naming, reading, and the dyslexias: A longitudinal overview." *Annals of Dyslexia*, 34, 87-115.

Wolf, M. (1986). "Rapid alternating stimulus naming in the developmental dyslexias." *Brain and Language*, 27, 360-379.

Wolf, M. & Denckla, M.B. (2005) *RAN/RAS: Rapid automatized naming and rapid alternating stimulus tests*. Pro-Ed.

Wong, P.C.M., Nusbaum, H.C., Small, S.L. (2004). "Neural bases of talker normalization." *Journal of Cognitive Neuroscience*, 16, 1173-1184.

Woodcock, R.W. (1998). *Woodcock Reading Mastery Tests – Revised/Normative Update (WRMT-R/NU)*. Circle Pines, MN: American Guidance Service.

Woodcock, R.W. *et al.* (2001). *Woodcock-Johnson Test of Cognitive Abilities III-NU*.

Ziegler, J.C. & Goswami, U. (2005). "Reading acquisition, developmental dyslexia, and skilled reading across languages: A psycholinguistic grain size theory" *Psychological Bulletin*, 131, 3-29.

Ziegler, J.C., Pech-Georgel, C., George, F., & Lorenzi, C. (2009). "Speech-perception-in-noise deficits in dyslexia." *Developmental Science*, 12, 732-745.