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Genes for reading and spelling

Timothy C. Bates*
University of Edinburgh, Scotland

This article reviews research on the behavioral and molecular genetics of reading and, where available, spelling. Recent research is summarized, suggesting that reading and spelling appear to share a common genetic basis, and that dyslexia lies on a genetic continuum with normal variance in reading skill. Research also suggests that while many of the genes involved in reading disorder affect all forms of reading, some genes are specific for processing irregular words, while others are specific for non-word or grapheme–phoneme processing, forming a genetic basis for the clinical distinction between surface and phonological dyslexia. Advances in molecular genetics mean that identifying specific genes for reading is now a practical project, and to date 11 chromosomal regions have been associated with reading or spelling and these findings are reviewed. Finally data are presented on the genetic relationship of dyslexia to other developmental disorders including Autism and ADHD, and reasons for this overlap or comorbidity are discussed. Gene discovery is at a point where precise biochemical effects underlying dyslexia can be understood, findings that will have an important impact not only for neuropsychology and neuroscience but also for psychological practice.

Introduction

Despite adequate intelligence, education and social environment, approximately 8% of children experience specific reading deficits or 'dyslexias' (Shaywitz *et al.*, 1990). While this serious clinical condition begins in childhood, its effects continue into adulthood, both in terms of ongoing reading and spelling deficits (Bates *et al.*, 2004a) and serious social impacts, probably due to both comorbidity with disorders such as attention deficit, as well as from negative environmental feedback (Maughan *et al.*, 1996).

Disorders of written communication, then, are both common and, often, refractory to normal educational experience. This essay reviews the role of genetics in explaining these individual differences in reading and spelling. The strong role of genes emerges clearly and consistently from the many studies now available

*Department of Psychology, University of Edinburgh, George Square, Edinburgh EH8 9JZ, Scotland. Email: tim.bates@ed.ac.uk

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(DeFries *et al.*, 1987) and for this reason this review concentrates on information from large-scale twin studies about the *structure* of the genetic influences on reading and spelling: their overlap and specificity, beginning with studies of twins where one or both have a reading disorder, and concluding with normal unselected samples. The second section reviews exciting progress in moving to identify the particular variant genes underlying human written language ability and disorder, highlighting 10 regions shown to be linked to reading disorder, again beginning in clinically ascertained samples and concluding with evidence from a large normal group that the regions linked to dyslexia are also implicated in normal variation in reading ability. In discussing the behavioral and molecular genetics of reading, we review the genetic overlap between reading and other disorders such as Autism. The review concludes with a summary of this new knowledge regarding the structure of reading genetics, the continuity of dyslexia with both normal reading differences and with other distinct diagnostic categories.

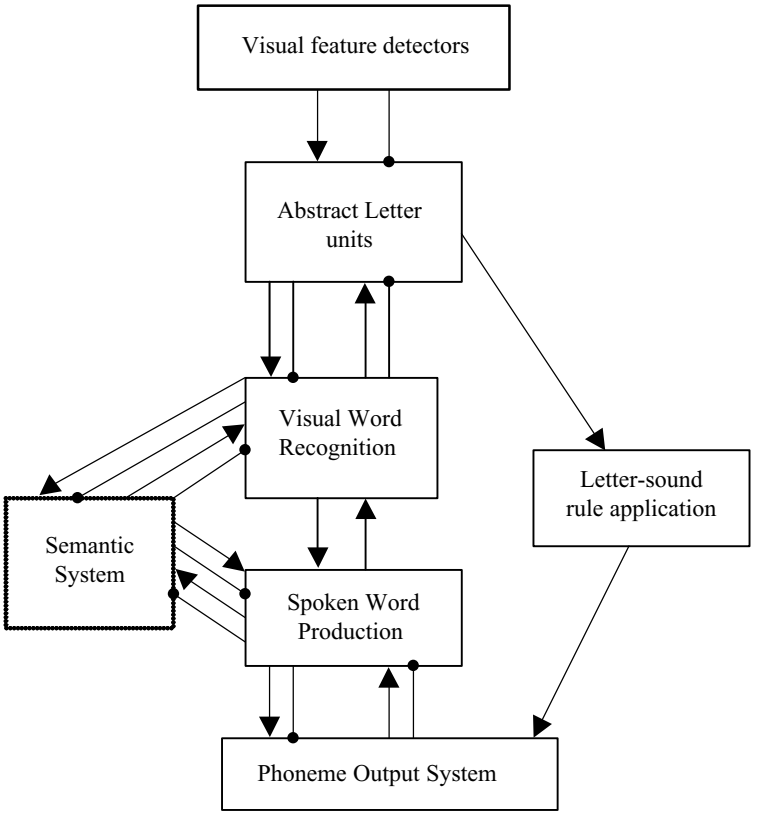
As a preparatory note, while this paper focuses on genetic research this does not deny the direct role of the environment or of the environment in interaction with genetic vulnerability. Rather, it is hoped, the review highlights the need and potential for an understanding of the genetic structure and basis of reading to advance clinical treatment. The genetic data are of particular interest because they remain less widely known, and yet contain surprising findings on the strength of the role of genes on reading, and on the genetic basis for distinctions made with dyslexia as well as genetic commonalities what appear, behaviorally, to be quite distinct phenotypes. Secondly, it is beyond the scope of this paper to cover the bases of quantitative or molecular genetics. For this purpose, readers are referred to excellent tutorial presentations available elsewhere (Plomin *et al.*, 2001).

Next a very brief overview of the phenotype—the clinical presentation of dyslexia, is given, before reviewing behavioral heritability research on reading disorder in twin samples.

Dyslexia as a phenotype

The two major subtypes of reading disorder identified clinically are surface and phonological dyslexia (Castles *et al.*, 2006). Surface dyslexia presents as affecting lexical processing, and can be assessed by examining performance on reading out-loud of irregular words, such as 'yacht', which cannot be correctly pronounced based on regular grapheme–phonological correspondences. Poor performance suggests an inability to store or access the sounds associated with familiar words, in other words inability to develop and or access a lexical store.

The second major type of dyslexia involves poor non-lexical reading thought to be due to problems developing a system to process the grapheme–phoneme correspondences that characterize most words in many languages. This 'phonological' dyslexia results in a reduction in phonological decoding ability, defined as the translation of written words without meaning cues into spoken words and typically assessed by reading out-loud of written non-words (character strings which, while possessing a



Note. Arrowed connections represent excitatory links and ball-ends show inhibitory connections. In this context, excitatory connections act to increase activation in their target, while inhibitory connections act to decrease target activity.

Figure 1. Dual route cascaded model of reading aloud (Coltheart *et al.*, 2001)

legal phonology, are not a word in the test language, for instance 'slint' or 'breek' in English). These two systems are shown in Figure 1, as modeled by the dual route cascaded model of reading (Coltheart *et al.*, 2001).

Regular words such as 'next' can be read aloud correctly by both the lexical and non-lexical reading systems. However these systems have important functional distinctions during development. Because the non-lexical route uses a system of grapheme–phoneme transformation rules, it can also pronounce regular words that have not previously been seen, and can thus serve as a self-teaching system (Share, 1995). This system will mispronounce novel irregular words but even in this case it may be of self-teaching value if the mispronunciation allows the learner to guess the correct pronunciation by comparison with words in the auditory lexicon. An important distinction between the routes of the dual route model is that the non-lexical

system does not have access to semantic support. For this reason, it cannot disambiguate homophones in text: given the sentence 'the bear skin was cold', the non-lexical system cannot decode lexical information that would allow the semantic system to understand that the skin referred to is that of a bear, not 'bare' or uncovered skin.

It is important to note that most cases show affection on both types of task (Castles & Coltheart, 1993), but also that pure cases of surface and phonological dyslexia are present in the normal population (Castles *et al.*, 2006). It also should be acknowledged that, while irregular and non-word stimuli are widely recognized as stressing the reading system in different ways, explanations and models of the architecture underlying the importance of these kinds of reading vary. Some models are compatible with a dual route architecture but emphasize different functions, for instance the lexical constituency model which emphasizes semantics and word identification, rather than focusing on naming (Perfetti *et al.*, 2005), or else focus on a more basic process underlying reading performance such as speed of automatized processing in the double-deficit account of dyslexia (Wolf *et al.*, 2000). Other models, though quite different in form, also suggest that two routes are revealed in the processing of irregular and non-word material: for instance the connectionist 'triangle' model of reading (Plaut *et al.*, 1996) which has two routes for successful reading aloud, but suggests that surface dyslexia arises not from a lexical deficit but rather from semantic damage. Finally, some theorists even suggest that surface dyslexia does not exist (Ziegler & Goswami, 2005).

Next we review evidence for the importance of genetics on the acquisition of skilled reading.

Heritability

The earliest researchers in reading noted that dyslexia was familial: it tended to affect more than one member of family and a family history of reading disorder was present in most cases (Thomas, 1905; Hallgren, 1950). In this circumstance, either shared environment (the family's rearing practices, culture, shared exposure to the physical environment), or shared genes are candidate causal agents in determining reading and the family resemblance cannot shed light on the relative magnitude of these causes. To learn more, a genetically informative sample is required: twins, adoptees, or other family types in which the normally confounded factors of rearing environment and genetic inheritance are systematically varied. In a twin sample the role of genes, of shared environment, and of unique effects such as measurement error can be made apparent by comparing the variance between families (in which rearing practices or effects of school or SES could appear) to within-family differences between twins who share all their genetic material (monozygotic or MZ) or only half (DZ dyzygotic): increased MZ over DZ similarity being evidence for genetic influences. By now numerous systematic studies of the symptoms and incidence of dyslexia have been completed in large twin studies and these are briefly reviewed below.

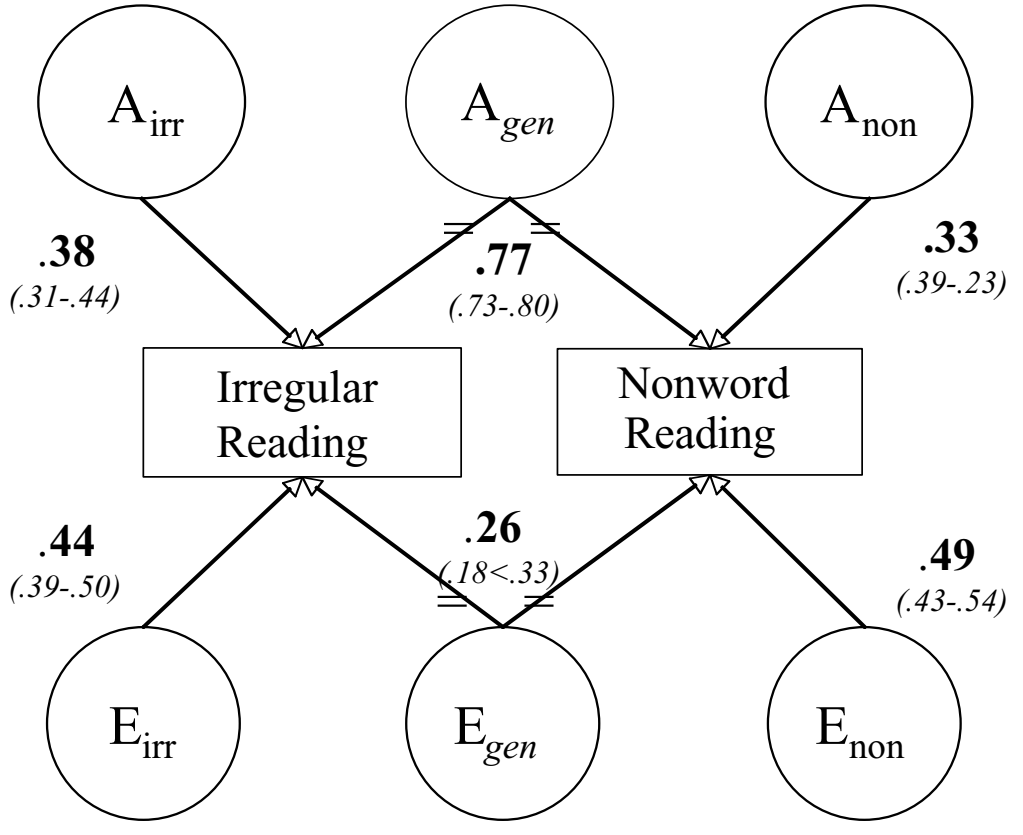
Heritability and the effects of age and gender

Earlier, small twin studies suggested that up to half of reading variance was due to genetic differences. It also appeared from these pioneering studies that non-lexical processing might be more strongly heritable, with lexical processing being more influenced by environment (Olson *et al.*, 1989; Stevenson, 1991). Subsequently, much larger studies now suggest that by adolescence heritability for both surface and phonological reading disorders is over 7% (Bates *et al.*, 2004a). This strong heritability emerges from pre-school onward (Olson & Byrne, 2005), with studies of the very youngest readers suggesting that shared environment does exert a significant influence prior to the age of 4-years-old (Byrne *et al.*, 2002), but that by age 8- or 9-years and above, the effects of shared family environment reduce to zero, and are replaced with increases in genetic effects (Tiu *et al.*, 2004). In addition to the effects of age during development, the role of sex in determining reading/dyslexia is an important and open topic, especially given recent reports that males are more at risk (Rutter *et al.*, 2004) and that severe risk is more highly heritable in males at least before age 8-years (Harlaar *et al.*, 2005). However, several studies point to a view that after 8-years, males are no more at risk, finding no qualitative, or quantitative sex differences (Bates *et al.*, 2004a; Wadsworth & DeFries, 2006). More research is needed in this area, given the contradictory state of data and clinical risk rates, which are indisputably elevated for males.

Specificity and generalist genes

So, if reading and spelling are heritable is there any structure to this genetic variance? Having focused on the distinction of surface and phonological dyslexia, and the dual route architecture which produces these dissociable forms of reading disorder, an obvious question is: are some genes specific for particular components of the reading system? This question has not been a focus of behavior genetic research, which has instead highlighted the general, non-specific genetic basis for reading and cognition. Behavioral modeling suggests that while most genes affect both forms of reading (Plomin & Kovas, 2005), some genes must be specific for lexical or non-lexical processing (Bates *et al.*, 2004a, b).

The hypothesis that there are genes specific for lexical and non-lexical reading has been tested by our own research group in Queensland (Bates *et al.*, 2006a), and results from this study are shown in Figure 2. As can be seen from Figure 2, the majority of genetic effects are general, affecting all forms of reading. However, it can also be seen that there are distinct genetic effects controlling processes specific to irregular word reading (thought to be related to the development of a lexicon) and others specific for non-word processing—the grapheme–phoneme conversion process. So from a clinical point of view, it can be expected that most cases of reading disorder will show affection of both surface and phonological processing. Individuals may also be expected, however, to have specific strengths and weaknesses, corresponding to differences in this genetic dual architecture of dyslexia. Some will



Note. Airr is Additive genetic effects for lexical processing; A_{gen} is general Additive genetic effects for reading; A_{non} is Additive genetic effects for non-lexical processing. E variables are the non-shared environmental effects on reading.

Figure 2. A dual route genetic model of reading (from Bates *et al.*, 2006, with permission)

therefore respond best to practice with grapheme–phoneme correspondences, and some to flashcard type lexical practice.

Comorbidity

Just as genetics can tease apart components of reading, genetics can also explain in part why dyslexia is associated with other disorders: the problem of co-morbidity. This is an important issue, and one that has to date received too few research resources. Again, since the earliest systematic studies (Hallgren, 1950) dyslexia has been shown to co-occur with speech and language disorder (Snowling, 2001) and with cognitive control and behavioral problems including ADHD (Gayan *et al.*, 2005) as well, of course, as autism which involves a language deficit. There is reason, then, to expect that genes implicated in these disorders may show some

association with dyslexia. Several possible causes of these associations are plausible, and it is at present unclear which is correct. Genes affecting reading may be 'pleiotropic', that is they may have 'side effects' on systems other than reading, unrelated to their role in reading per se. Alternatively, as reading depends on functionality in multiple systems (language, vision, and attention to note just a few), dyslexia will co-occur with other disorders dependent on any one or more of these systems. Finally, dyslexia may itself be a component of some more severe disorders. Autism appears to be a likely case in which a diagnosis is given when a child is affected by several unrelated disorders, including reading or language disorder. In this case, the complex disorder would be better thought of in terms of these independent disease entities and their interaction. More work is needed in this area, aimed at decomposing the general and specific genetic components of developmental disorders. Genetics can be a powerful guide in this process (Plomin & Kovas, 2005), and the field of genetic taxonomy, while in its infancy, promises significant benefits for rational diagnosis and treatment.

Gene discovery

The work above has shown that dyslexia is polygenic (with several genes at work). Each of these single genes is known as a quantitative trait locus or 'QTL'. Despite the fact that the biochemical effect of these genes on neural reading systems is likely to be diverse and, at present, is almost completely unknown (Eckert *et al.*, 2003), the fact that that these QTLs influence a trait will lead to a continuum of liability and the QTLs themselves can be detected via their effect on behavior.

While the genetic cause of some medical disorders has come from identifying rare genes capable of causing the disorder on their own, no such genes have been identified for dyslexia. When, as in the case of reading, few candidate genes have been described, the search for genes must proceed via genome-wide search. An optimal strategy to achieve this would involve typing all subjects at each of the three billion DNA base-pairs comprising each individual's genome—a prohibitive challenge at current costs. Thankfully, some short cuts to localizing genes exist, based on the fact that genes in close proximity to each other tend to be transmitted together for long periods of time. During transmission of our DNA from parent to offsping, only a few hundred 'crossing over' changes occur, leading to large segments of DNA containing several dozen genes being transmitted as if wrapped together in a single package. This in turn means that a single marker can be used to track the transmission of all genes within that package. This paradigm is known as linkage and allows just a few hundred markers to accurately track gene effects within families (see Carlson *et al.*, 2004 for a review). There is a second method for gene discovery which is based on similar logic to that involved in linkage, but which relies instead on the very much smaller linkages which are created at the time the particular QTL comes into existence (by mutation). This novel QTL will be transmitted together with all of the surrounding chromosomes of the founder in whom the mutation occurs, and this association will be visible not just in immediate family members (as in linkage) but in

all members of a population sharing this founder. Repeated crossing over rapidly breaks down distant associations, so that after a few generations only very short range linkage disequilibrium exists (connecting perhaps only one or two genes nearby the mutation), which ensures that association are very sensitive to location, and to genes of very small effect. Linkage and association, then, are complementary strategies for research.

To date, no genome-wide direct association study for reading has yet been undertaken although several groups are working on generating the very large databases of genetic information on each participant (upwards of 100,000 markers per person) necessary to conduct such studies. Several linkage studies have, however, been completed, and these are introduced below, along with subsequent gene identification work.

As indicated, linkage identifies the approximate location of QTLs by tracking the sharing of large chromosomal segments in closely related individuals. Because close relatives share long regions of DNA, systematic coverage is achieved with as few as 400 markers (Carlson *et al.*, 2004). However, because linkage relies on the co-transmission of large segments of DNA, it can identify only the approximate location of a gene of interest. Much more work is required to understand which of the several dozen candidate genes within a linkage peak is responsible for the linkage. In addition to this lack of sensitivity to precise location, a major limitation of linkage is that it requires extremely large numbers of subjects to detect genes of small effect (Risch, 1990): this is because a gene with a small effect size (< 3–4% of variance) will often be present at all levels of a phenotype.

Dyslexia was one of the very first quantitative traits to be studied using linkage and the strategy has been successful beyond all predictions, with 11 regions located across the genome, and association testing proceeding in several of them. A recent review has covered these findings in depth (Fisher & DeFries, 2002) and here we cover the results in less depth, and bring the reader up to date with work since 2002.

Chromosomes are numbered in accordance with their length, and the shorter and longer arms either side of the chromosome's centromere are termed 'p' and 'q' respectively, with subsequent numerals denoting successive bands which stain dark in pictures of the chromosome. Regions which appear to be replicable or strong are given a name, with dyslexia genes being labeled in numerical sequence beginning 'DYX'. Knowing this nomenclature, the current regions of interest are as follows: 1p34-36 (Rabin *et al.*, 1993; Grigorenko *et al.*, 2001; Tzenova *et al.*, 2004), 2p15 (Fagerheim, 1999; Kaplan *et al.*, 2002b; Francks *et al.*, 2002; Petryshen *et al.*, 2002; Kaminen *et al.*, 2003; Chapman *et al.*, 2004;), 2q22 (Raskind *et al.*, 2005), 3p12-q13 (Nopola-Hemmi *et al.*, 2001; Taipale *et al.*, 2003), 6p22 (Cardon *et al.*, 1994; Cardon *et al.*, 1995; Grigorenko *et al.*, 1997; Fisher *et al.*, 1999; Gayan *et al.*, 1999; Grigorenko *et al.*, 2003; Turic *et al.*, 2003; Chapman *et al.*, 2004), 6q11 (Petryshen *et al.*, 2001), 7q32 (Kaminen *et al.*, 2003), 11p15 (Hsiung *et al.*, 2004), 15q21 (Grigorenko *et al.*, 1997; Schulte-Körne *et al.*, 1998; Nothen *et al.*, 1999; Morris *et al.*, 2000; Nopola-Hemmi *et al.*, 2000), 18p21 (Fisher *et al.*, 2002; Marlow *et al.*, 2003; Chapman *et al.*, 2004) and Xq26 (Fisher *et al.*, 2002; de Kovel *et al.*, 2004).

The first reported linkage for dyslexia (indeed the first linkage for any complex trait) was to chromosome 15 (Smith *et al.*, 1983) and has been replicated in three separate laboratories for a categorical (Grigorenko *et al.*, 1997) and continuous measures of single word reading (Chapman *et al.*, 2004) for spelling (Schulte-Körne *et al.*, 1998; Nothen *et al.*, 1999). Two studies failed to replicate this linkage (Bisgaard *et al.*, 1987; Lubs, 1991), but this is to be expected even for a true gene as mutations are not expected to present in all populations.

Further support for chromosome 15q21 being involved in written language processing came from the discovery of a translocation in a single family associated with both verbal short-term memory and rapid automatized naming. A candidate gene in this region was proposed by Taipale *et al.* (2003) based on evidence that two base pairs within this gene were altered in their dyslexia sample. The gene is expressed in cortical neurons and white matter glial cells (Taipale *et al.*, 2003). Two studies have replicated the association of 15q21 to dyslexia (Morris *et al.*, 2004; Wigg *et al.*, 2004), but three studies so far have failed (Scerri *et al.*, 2004; Cope *et al.*, 2005; Marino *et al.*, 2005). In conclusion, while the location of this linkage has been replicable in at least some samples, the phenotypic specificity of this linkage and the gene itself require further study.

The second region linked to dyslexia was reported by Cardon *et al.* (1994, 1995) and has since been replicated widely, both by this group (Fisher *et al.*, 1999; Gayan *et al.*, 1999; Kaplan *et al.*, 2002b) and other laboratories (Grigorenko *et al.*, 2000; Turic *et al.*, 2003). While Grigorenko *et al.* (2000) suggested this gene might be specific for phonological awareness, multivariate analyses suggest strongly that this region is not specific to one or other phenotype (Marlow *et al.*, 2003). The gene appears now to be linked to a broad range of reading traits including single-word reading, spelling, phonological and orthographic accuracy and rapid automatized naming but not broader phenotypes such as vocabulary or attention deficit hyperactivity disorder (Turic *et al.*, 2003). Not all studies have found the 6p linkage (Field & Kaplan, 1998; Petryshen *et al.*, 2000; Chapman *et al.*, 2004). The precise phenotype linked at 6p and the populations in which it is found therefore remain uncertain. Based on the pattern of success and failure to replicate (mostly using speeded and un-speeded tasks respectively) 6p may be related to processes determining the speed of automatized naming, rather than accuracy of reading. Most exciting, the 6p region has begun to reveal clear candidate genes, most notably KIAA0319 and DCDC2 (Francks *et al.*, 2004; Cope *et al.*, 2005) and ongoing research should clarify the role of these genes in creating risk for reading at a cellular level, which would represent a break through in our understanding of reading disorder.

Additional genetic loci

Since the first two reports, a number of additional sites have been implicated in reading, as summarized in the introductory paragraph of this section. It is of interest to note that DYX3 on chromosome 2 (Fagerheim, 1999) & DYX5 on chromosome 3 (Nopola-Hemmi *et al.*, 2001) were discovered based on pedigrees in which

dyslexia appeared to be inherited as an autosomal dominant trait. This highlights the value of even small pedigrees where the degree of affection is severe and penetrant to speed gene discovery: active collaboration between those in contact with such families and genetics researchers could do much to hasten the discovery of the genes for human language disorder.

In the first two genome-wide scans reported for reading, Fisher *et al.* (2002) reported a linkage at chromosome 18p21. This was present in both a UK sample of 195 sib-pairs ascertained on the basis of one dyslexic child and at least one sibling with reading problems requiring an IQ discrepancy, and in 180 sib-pairs from the Colorado twin sample ascertained on the basis of one member having a school history of reading difficulty, irrespective of IQ discrepancy, suggesting that it is a fairly robust linkage with respect to diagnostic criteria. The discovery of linkage on chromosome 11p15 highlights the importance of the comorbidity of dyslexia with other disorders, noted above. This region was examined because of the association of dyslexia and ADHD (Willcutt & Pennington, 2000) and the association of dopamine D4 receptor (DRD4) polymorphisms with ADHD (Faraone *et al.*, 2005). Hsiung *et al.* (2004) evaluated markers around the DRD4 locus in 100 families with two or more affected siblings. Dyslexia was associated with polymorphisms surrounding the DRD4 region, suggesting that this, or nearby genes may influence dyslexia. Another molecular finding which highlights a phenotypic observation is the recent report of X chromosome involvement by de Kovel *et al.* (2004) who reported linkage to Xq27.3 in 29 individuals from a single Dutch family segregating dyslexia with an autosomal dominant pattern for discrepancy-score based dyslexia. The X-chromosome is relatively gene-poor, and the region implicated in de Kovel's study contains only 11 confirmed genes, and the linkage is close to one reported by Fisher *et al.* (2002) in their genome-wide scan. There is hope for a new gene for reading in this region which might shed light on the matter of sex differences in reading disorder.

Finally, Raskind *et al.* (2005) recently reported a novel linkage for phonological decoding efficiency at 2q. This report is of interest here, for highlighting the potential top find genes specific for one form of dyslexia. Raskind contrasted analyses of phonological decoding efficiency from the TOWRE and Woodcock Johnson word attack tests. The former is a measure of accuracy and speed of phonological decoding, whereas the latter is un-speeded and assesses accuracy alone. A highly suggestive linkage was found at C2q for decoding efficiency but this peak was absent for word attack. The authors concluded that the C2q locus influences the speed but not accuracy of phonological decoding, a finding reminiscent of the double-deficit hypothesis (Wolf *et al.*, 2000).

As a final example of recent research on the molecular basis of reading, Bates *et al.* (Bates *et al.*, 2006b) conducted the first genome-wide scan for dyslexia in over 400 unselected normal families. They reported replication support for DYX1 (15q), DYX4 (6q), DYX6 (18p21), and for 7q32 (Kaminen et al., 2003). In addition, lower-level support was found for DYX3 (2p15), DYX5 (3p12), DYX8 (1p) and DYX9 (Xq27) as well as for a region close to the 2q locus reported by Raskind *et al.*

(2005). Thus support was found in this unselected sample for all previous linkages barring DYX2 (6p21) and DYX7 (11p15), strongly suggesting that the linkages are valid, strong, and active in the normal population as well as selected dyslexic samples.

It can be seen, then, that molecular research both feeds off and helps us to understand patterns of behavioral variance such as sex differences, and associations and dissociations between tests and clinical categories. It further suggests that the genes for dyslexia are also active in defining normal variance in reading ability.

Comorbidity and generalist genes

An interesting feature of these linkages for reading is their convergence with linkage in other clinical disorders. For instance, 2q21-33 holds a gene for autism, (IMGSAC, 2001) and has been linked to cognitive deficits in childhood-onset schizophrenia (Rapoport *et al.*, 2005), while the 6p region associated with dyslexia, especially speeded reading measures (Kaplan *et* al., 2002a) has recently been reported to be linked to measures of IQ (Posthuma *et al.*, 2005). This study also found linkage for spatial-processing ability (performance IQ) in the 2q region, but also reported linkage at this region to the Cambridge Contextual Reading Test. Likewise the region of chromosome 15 associated with DYX1 contains a putative attention-deficit/hyperactivity gene as well as the candidate DYX1C1 gene. Some links between reading and language have been suggested: for instance Kaminen *et al.* (2003) reported suggestive support for a locus on 7q32 possibly at the FOXP2 locus: a gene which is responsible for a syndrome of dysarthric agrammatism (MacDermot *et al.*, 2005). Also close by is an autism locus AUTS2 (Sultana *et al.*, 2002). Of course until the actual genes are known, it remains possible that these co-occurrences of linkage represent different genes in mutual proximity. Perhaps more informative are failures to find overlapping linkages. It is of great interest, for instance, that despite theoretical suggestions that specific language disorders (not reviewed here) determine much of dyslexia, the linkages for SLI reported to date do not overlap with those for dyslexia (cf. SLI Consortium, 2004).

Conclusion

The implications of genetic research on dyslexia reviewed above reach into cognitive theory and clinical practice. For example, genetic research suggests both that the diagnostic distinction between surface and phonological dyslexia is genetic as well as behavioral. This suggests that the disorders may need specific treatments. The research also points to the fact that many of the genes active in reading disorders are largely generalists rather than specialists: they cut across traditional diagnostic categories such as attention deficit and autism as well as general intelligence and specific language processing deficits.

At first glance, this finding of genes which are specific for particular subcomponents of a single disorder, and of genes which cut across entire diagnostic

categories appears somewhat contradictory. Are the diagnostic categories valid or not? Are their components of disorder or not? Is there just one general childhood risk factor, or many interacting factors which determine a specific disorder profile? The answer is of course that this situation mirrors the clinical presentation: we observe both comorbidity and specific individual profiles. The resolution of the genetic findings is that, from a genetic perspective, language, reading, and mathematics disabilities are not wholly distinct diagnostic entities but are embedded within an overarching network of genetic effects. Some of these genetic effects exert a strong influence over multiple behavioral symptoms, and lead to high levels of comorbidity. Others, however are quite precise in their effects, and it is these which define the unique features on which differential diagnoses are based.

Although understanding the causes of dyslexia will not necessarily lead to cures, it seems likely that identification of the genes involved in reading disorder, with several very promising candidates already under study, will help researchers to address the biological and biochemical deficits that lead to dyslexia, or at the very least, to identify children at risk well before the normal period when a failure to read has already occurred, possibly identifying risk many years before this time, and allowing a program of risk mitigation to be put in place. It is hoped that genetic research can advance the prevention of dyslexia, avoiding the delays and deepening our understanding of individual causes and risks, thus averting the many social and personal costs imposed on so many children at present.

Notes on contributor

Timothy Bates holds a Readership in the Department of Psychology at the University of Edinburgh. Following his Ph.D., he took up a lectureship at Macquarie University in Sydney in 1996 subsequently joining the Macquarie Centre for Cognitive Science in 1999, where he worked until 2005. His research interests lie in individual differences in cognition, including intelligence, reading and language.

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and genome-wide data replicate loci at DYX1, DYX4, DYX6 and 7q32, with weaker support for DYX3 DYX5 DYX8, DYX9, and no evidence for DYX2 or DYX7. Genome-wide suggestive evidence for novel linkage on chromosomes 4 and 17. *submitted.*

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