

PLINX204 PSYCHOLINGUISTICS

LANGUAGE ACQUISITION – 2006 - 7

Molecular genetic evidence (2)

QTL Analysis and Dyslexia

Basic reading: Stromswold, 2001; Plomin et al, 2000, 2002; Newbury et al, 2005; Snowling, 2000.

Additional reading: Any of: Fisher et al, 1999; Francks et al, 2004; Stein et al, 2004; Suresh et al, 2006; Lefly & Pennington, 1996; Gallagher et al, 2000.

1. There is a contrast between single-gene effects such as that of FOXP2 in the KE family and multiple gene effects which are characteristic of e.g. stuttering and **dyslexia** (aspects of spoken and written language respectively), and other gradient phenomena. Such effects are typically investigated on the basis of QTL (Quantitative Trait Locus) analysis. A QTL is a region of DNA associated with a particular phenotypic trait (e.g. plant height). Though not necessarily genes themselves, QTLs are stretches of DNA that are closely linked to the genes that underlie the trait in question.

2. **Dyslexia**: “a developmental disorder selectively affecting a child’s ability to learn to read and write ... affecting boys more often than girls” (and left-handers more often than right-handers) (*Oxford Concise Medical Dictionary*). For a basic introduction, see Snowling, 2000. Dyslexia is frequently (incidence 50%) associated with speech and language impairment (Lefly & Pennington, 1996:52). Hence, for this 50%:

3. There are linguistic predictors of reading difficulty: specifically, a problem in phonological coding reflected in deficiencies in phoneme perception, phoneme awareness, lexical retrieval, verbal Short Term Memory, etc.

sleep/slow vs. crunch/bunch

hat/mat/fat/man vs. pin/fin/sit/sin

boot/barn/buy/ear

What does c-a-t spell?

What does ‘cat’ have that ‘at’ lacks?

NB these different deficiencies may dissociate in all possible combinations.

4. In contradistinction to this linguistic deficit hypothesis for dyslexia, some have claimed that it is a function of a more general problem with auditory coding, rather than a defect specific to reading (or language). (See Tallal, 1984; Mody *et al*, 1997; Denenberg, 1999). Evidence comes from tests of categorical perception of verbal and non-verbal stimuli, differences in short term memory for verbal and nonverbal stimuli, perception under noisy conditions, etc. The balance of evidence supports the claim that, at least for some subjects, the dyslexia is not a reflex of a more general auditory deficit - i.e. it is specific to speech. Nonetheless, the aetiology of typical dyslexia may include an auditory deficit.

5. Within dyslexia it is necessary to distinguish:

a. Developmental *vs.* Acquired dyslexia

Only developmental dyslexia is relevant to the debate about genetic determination of the language faculty, though the other is fascinating, and it is puzzling that there is no obvious developmental equivalent of ‘deep’ dyslexia.

b. Surface *vs.* Deep dyslexia

(Coltheart *et al.*, 1987, esp. pp. 433-436) - “Lemons are sweet” > ‘Limes are sour’).

c. Surface *vs.* Phonological dyslexia

Surface dyslexics can read regular words (e.g. *cave*) and regular non-words (e.g. *mave*), but fail on irregular words (e.g. *psalm*, *yacht*); phonological dyslexics can read regular (e.g. *cave*) and irregular (e.g. *psalm*, *yacht*) words, but fail on non-words (e.g. *mave*).

6. Standard explanation: for typically-developing children there is assumed to be a ‘dual-route’ for reading – ‘look-up’ (necessary for the correct identification of irregular words) and ‘sounding out’ (necessary for the correct identification of novel [regular] words). With dyslexics, either or both of these routes may be disrupted.

7. Dyslexia is largely familial and heritable. “Family history alone is the best predictor ... of later dyslexia” (Lefly & Pennington, 1996:50).

a. The best evidence for heritability comes from twin studies: thus, MZ twins, one of whom has been diagnosed as dyslexic, will regress to the mean less than DZ twins (i.e. MZ twins show greater heritability) (Snowling, 2000:140).

b. Literacy delay correlates with familial ‘at-risk’ status for dyslexia: 57% incidence in at-risk group, 12% in control group (Gallagher et al, 2000:209).

c. Surprisingly, the surface and phonological forms of dyslexia are differentially susceptible to genetic aetiology. In two populations each of 322 children:

i. surface dyslexics showed heritability for reading of 0.31 with environmental variance of 0.63.

ii. phonological dyslexics showed heritability for reading of 0.67 with environmental variance of 0.27.

In other words there is a strong genetic component to phonological dyslexia, associated with a spoken language deficit. (Snowling, 2000:144).

d. Within phonological dyslexia there are striking dissociations between affected abilities:

i. Word recognition: heritability decreases as a function of age

ii. Spelling: heritability increases as a function of age

8. Given this variation, and since dyslexia has the properties of a continuum (there are degrees of severity in the condition), it qualifies as a quantitative trait. But, the familial determination could still be either Mendelian or due to a QTL. If it were Mendelian, there would be two potential modes of transmission:

- a. Autosomal dominant transmission
- b. X-linked recessive transmission

(a) can account for familial resemblance but fails to account for e.g. the fact that 20% of dyslexics do not have affected relatives. (b) is plausible when a condition occurs more often in males than in females, as in dyslexia, but (b) fails here because X-linked recessive transmission predicts the absence of father-to-son transmission (because sons inherit their X chromosome only from their mothers), and reading disability is transmitted from father to son as often as from mother to son. Further:

- c. Mendelian and QTL analyses of the familial determination make different predictions about the reading development of children from high-risk families that do not become dyslexic (Lefly & Pennington, 1996:50). The discrete (Mendelian) model predicts that they should be similar to low-risk controls. The continuous model predicts that they should be intermediate between dyslexics and low-risk controls. The continuous model makes the correct predictions.

9. Hence is it generally accepted that reading disability is caused by multiple genes and multiple environmental effects, and is plausibly due to one or several QTLs. Note that a particular QTL may be neither necessary nor sufficient for the phenotype in question.

10. The discovery of the first QTL for dyslexia: Rice (1996:xiii; Gayan *et al*, 1999; Lefly & Pennington, 1996:50f.). The first gene markers for dyslexia were found on the long arm of chromosome 15 (implicated in 30% of affected families). The locus probably contains 10 to 100 genes, only some of which are causally implicated in the phenotype. More recently (Fisher *et al*, 1999:146) analysis by means of sib-pair trait differences suggests the presence in 6p21.3 of a QTL influencing multiple components of dyslexia, in particular the reading of irregular words ($P = .0016$) and non-words ($P = .0024$). There may also be a translocation on chromosome 1. cf. (3) above.

11. **Stuttering.** (Suresh *et al*, 2006; Riaz *et al*, 2005).

Approximately half of stutterers have a family history of the disorder, but “Mendelian inheritance is typically not observed, supporting the view of stuttering as a complex [=QTL] trait” (Riaz *et al*, 2005:647). Investigation of 44 Pakistani families from Lahore showed evidence of linkage on chromosomes 1, 5, 7 and 12, but only 12 (specifically, close to PAH 109.47cM) gave systematic and major effects on all analyses.¹ Additional evidence implicating chromosome 18 is available from other studies, and there are

¹ The language used was not thought worthy of mention! {Actually, tests were conducted in Urdu and English, and no significant differences were found – D. Drayna, p.c.}.

significant effects on chromosomes 9 and 15, sex-specific linkage to chromosome 7 (males only) and chromosome 21 (females only); some effect from chromosome 2... Conclusion: "Given the complex genetics of stuttering, it is possible that alleles at numerous loci contribute to this phenotype" (Riaz et al, 2005:650).

12. Conclusion: Genetic determination of the language faculty is stunningly complex. Dyslexia and stuttering are relatively minor aspects of our linguistic abilities but are underpinned by the effects of vast numbers of genes distributed across many chromosomes.

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