

# Psych 3102

## Introduction to Behavior Genetics

### Lecture 17

#### Genetics of cognitive disabilities

#### Learning disorders

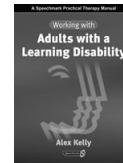
### Learning disorders

#### Diagnostic criteria

- achievement below expected for age, schooling, cognitive ability
- significantly interferes with achievement in life

Prevalence: 2-10% in general population  
5% in public schools

Types: written expressive disorder no genetic studies  
mathematics disorder moderate genetic influence  
+ overlap with reading disorder  
reading disorder 80% of all cases of learning disorders  
60-80% of cases are males (bias by schools?)



## Reading disability

- scoring 1.5 sd below mean for single-word decoding test
  - not explained by environmental deprivation, poor education etc., unexpected for IQ level of child
- dyslexia

- most studied learning disorder
- large family studies show a genetic component
- replicated studies have located QTLs

### Colorado Adoption Project

reading disability study Dick Olson, John D. Olson  
1044 individuals from 125 families containing a reading-disabled child + 125 matched control families

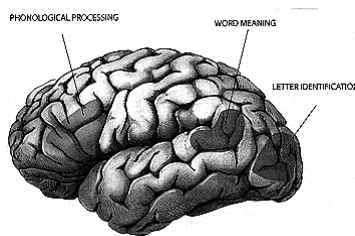
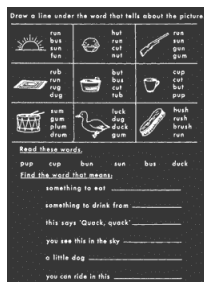


### Colorado Twin study

longitudinal study of reading disability  
250 twin pairs where one or both twins were reading disabled

## Word-reading deficit

- a quantitatively-measured component of reading disability
- Gayan & Olson (2002) Developmental Neurophysiology
- $h^2 = 54\% + \text{epistasis}$
- some specific alleles for disorder indicated by DF extremes analysis, but largely reading 'disorder' represents tail end of reading ability distribution
- $e^2 = 0.06\%$     $c^2 = 39\%$    complex environmental influence



## Locating genes for reading disability

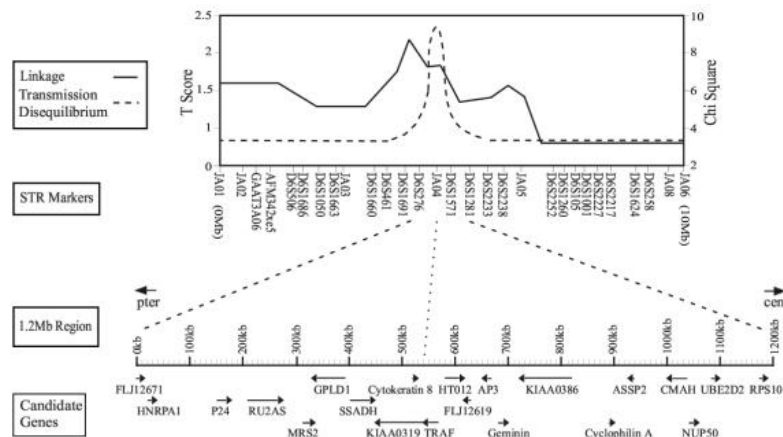
Cardon et al (Science, 1994) + many replications since

QTL linkage analysis using the sibpair allele-sharing method

- locates QTLs for the trait by looking for allelic variation at marker loci that influences trait variation among sib pairs
- made more powerful by selecting probands with extreme scores for reading disability

Located markers linked with reading disability on chromosome 6   2 loci p21.3 and p22.2

2 genes   DCDC2   KIAA0319



**Transmission disequilibrium and genetic linkage analyses of the 6p21.3 reading disability locus, regional STR markers and transcription map.** At the top of the figure is the result of the DeFries-Fulker linkage (T Score, solid line), and QTDT linkage disequilibrium (chi-square, dashed line) [14]. The location and order of the 29 STRs are shown below which identify a peak of transmission disequilibrium at marker JA04. Below the markers is a detailed representation of 1.2 Mb surrounding marker JA04. The 19 genes and 2 pseudogenes encoded in this region are shown with the telomere on the left and centromere on the right and their position and direction of transcription indicated by the arrows.

Currently 13 regions of genome being investigated after previous studies & recent whole genome scan implicated them in variation for reading & spelling measures.

From genes to behavior:

4 most replicated genes participate in brain development (neural migration)

Galaburda et al, Nature Neuroscience, 2006

- abnormalities in brain development reported in dyslexia
- comparable abnormalities induced in animal models cause auditory, cognitive deficits
- brain abnormalities thought to lead to phonological & auditory processing abnormalities & mode of action of these genes is suggested

**Possible reasons behind lack of replication for linkage studies on complex traits:**

- 1.
- 2.
- 3.
- 4.

Recent development: Multivariate analysis methods

- several phenotypic measures used rather than one (univariate) or 2 (bivariate)
- more power to detect linkage

Marlow et al (2003) – Reading disability

several correlated (0.38 – 0.80, most >0.5) measures of the phenotype

confirmed linkage to regions on chromosome 6 and 18