Psych 3102
Introduction to Behavior Genetics

Lecture 20

General Cognitive Ability – Developmental aspects

1. Changes in heritability during development

- does similarity between relatives change over time?

2. Influence of genes on development

- do genes contribute to changes during development?

3. Locating genes involved in general cognitive ability

- many genes of small effect, can methods be developed to allow them to be located?

1.Changes in heritability during development

- long-term stability after childhood (from age 5) is greater for g than for any other behavioral trait
- genetic influence seems to become more important over time
- gene expression seems to vary over a lifetime

Evidence from family and adoption studies — Colorado Adoption Project

- longitudinal study of parents and offspring
- measured for cognitive ability from infancy to adulthood

	Correlations	
Relationship	Infancy	Adolescence
Parent/offspring	0.18	0.30
AdoptiveP/offspring	0.08	0.03
BiolP/adoptedawayoffspring	0.12	0.37

- indicates gene influence increases over course of development
- little evidence for persistent effects of shared environment

Table 3 Parameter estimates resulting from the fit of a parsimonious model of genetic and cultural transmission to general cognitive ability data in the Colorado Adoption Project

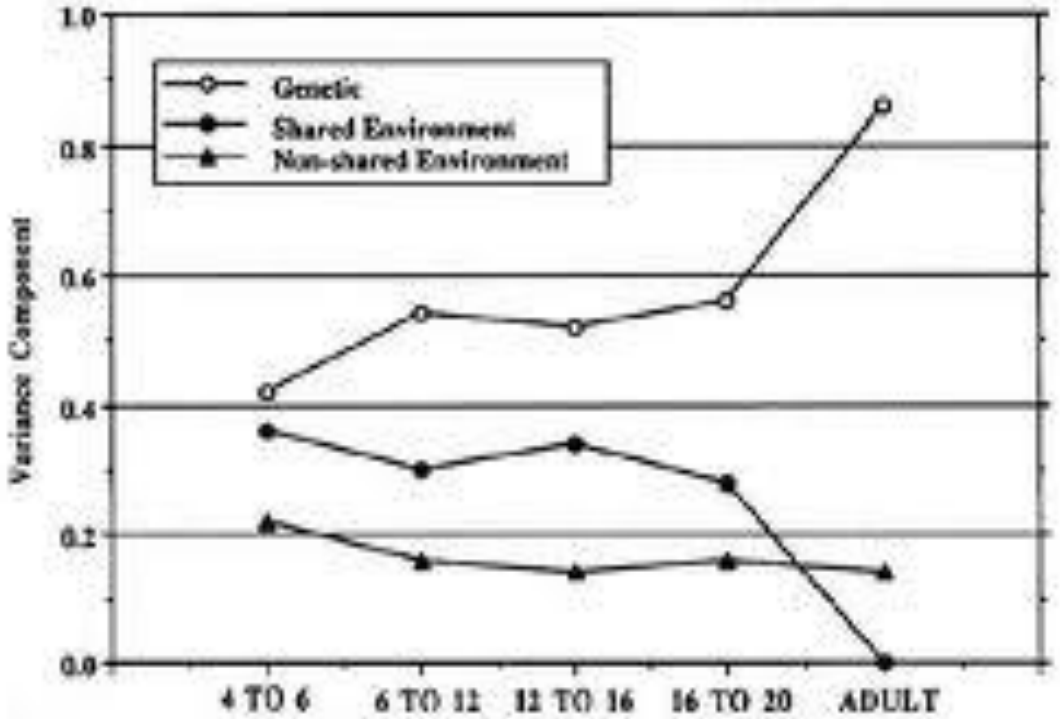
	Age in years				
Parameter	1	2	3	4	7
h^2	0.09	0.14	0.10	0.20	0.36
$m = f$	0.04	0.05	0.10	0.07	0.01
$p = q$	0.27	0.25	0.27	0.27	0.21
s	0.02	0.03	0.05	0.04	0.01
χ^2	33.52	32.86	29.84	30.13	25.48
d.f.	26	26	26	26	26
$P >$	0.10	0.10	0.20	0.20	0.40

Evidence from twin studies

Minnesota Twin Study

- comparison of MZs and DZs reared together, birth to adulthood

MZs and DZs start with more similar correlations (0.79, 0.59)
but difference goes up slightly early → mid-childhood (0.82, 0.59)
then up considerably into adulthood (0.86, 0.39)



IQ variance component estimates derived from published IQ twin correlations. Estimates are based on the standard assumptions used with the Falconer heritability formula (from McGue et al. 1993)

Louisville Twin Study

– similar study with similar results

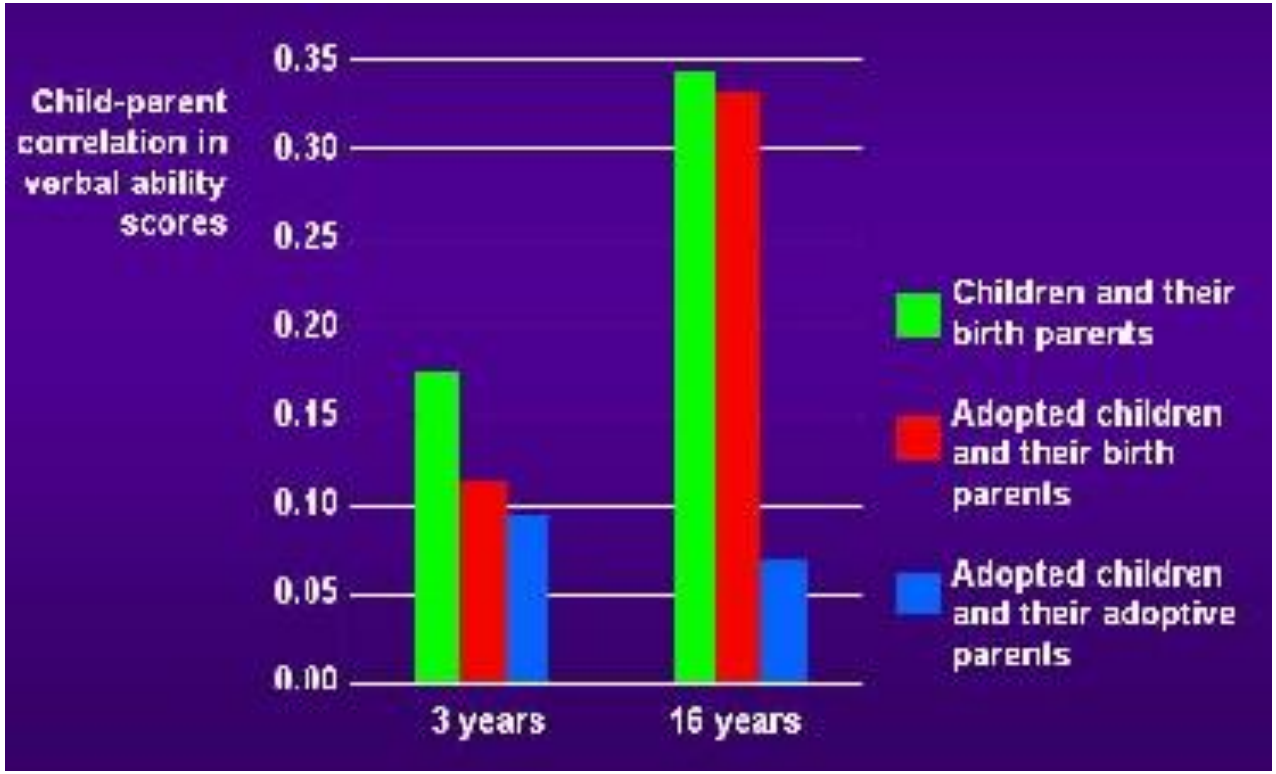
twin studies support results of adoption studies (see text)

- the older the subjects in the sample, the higher the heritability
- average $h^2 = 0.75$ after adolescence

Swedish Twin Study

MZ twins age 60, reared apart $h^2 = 0.80$

replicated with similar results at age 80


Child-parent correlation in verbal ability scores
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
3 years
16 years
Children and their birth parents
Adopted children and their birth parents
Adopted children and their adoptive parents

- all evidence points to increasing heritability with age

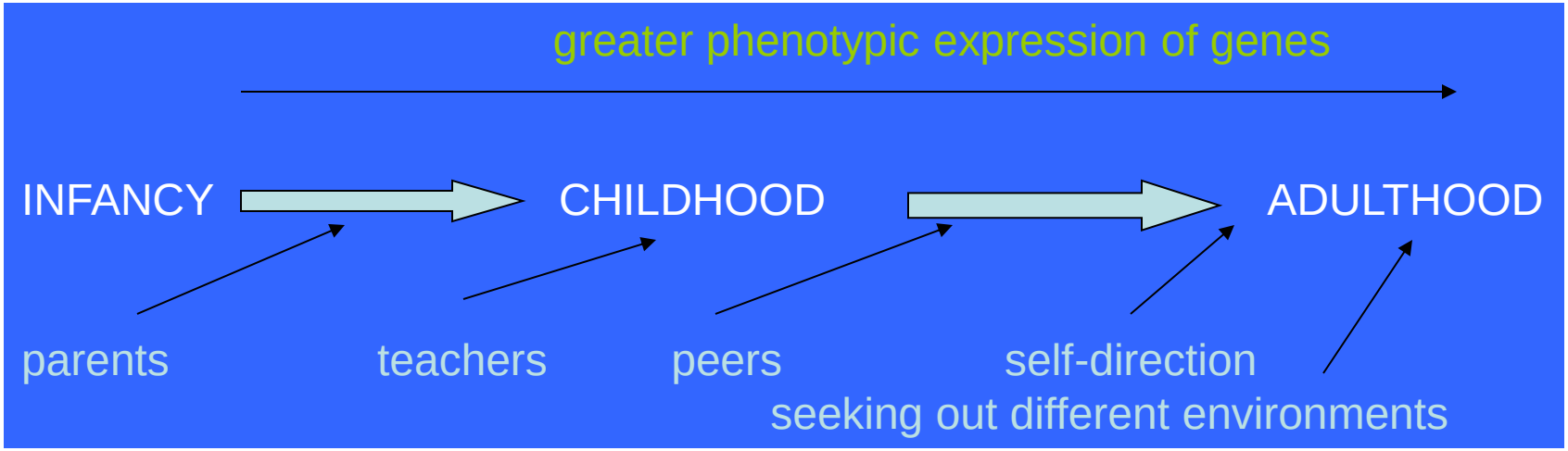
- **why?**

different genes expressed at different ages?

full phenotypic effect of genes not shown until adulthood?

lessening of environmental influences with age?

genotype/environment correlation and/or interaction may reinforce genetic differences



2. Changes in gene expression

- some gene effects can only occur when certain developmental milestones are reached

genes affecting processes involved in language

Evidence from longitudinal studies model-fitting analyses

Fulker et al (1993):

2 transition stages:

1. infancy → early childhood LANGUAGE DEVELOPMENT
2. early → mid-childhood FORMAL SCHOOLING

- most gene effects contribute to continuity, not change, over time
- some gene effects contribute to changes in the transition stages (text pages 168-169) See also Chapter 9

3. Locating genes for general cognitive ability

- many genes of small effect for cognition in normal range

- most success so far in locating genes with severe effects producing cognitive disability

Methods used:

knock-out gene studies in animals (eg.mice)

allelic-association studies of candidate genes in humans

full genome-scan linkage analyses in humans – but power is weak

Boosting power to detect loci of small effect

- use a HUGE sample 30-40,000 people

\+ use many thousands of markers spread across genome

- use an endophenotype (an 'intermediate' phenotype)

\- an indicator of a biological state manifest as part of a trait or disorder

\- for disorders, present in relatives to less extreme level

\- a quantitative measure , can be measured in general population

biomarkers: measures of substances found in blood, saliva, urine

neuromarkers: substances found in cerebrospinal fluid

other: anatomical measures (eg brain scans by MRI)
physiological measures (eg functional imaging of brain by fMRI,ERP)
behavioral tests

Properties of a good endophenotype

- provides a quantitative measure
- relatively cheap, easily and reliably measured
- always present, stable
- specificity specific to the disorder
- sensitivity identifies majority of those with disorder
- for genetic studies: needs to be heritable

Applications

- aid gene-locating studies
- act as risk factors, used to identify liability for a disorder
- aid in early detection of disorder, maybe before symptoms
- improve diagnosis, indicate severity

Endophenotypes for cognition:

1. size of head correlates 0.2 – 0.4 with IQ

2. brain size (MRI) correlates 0.51 with IQ, but sex differences

3. brain volume correlates 0.4 with full scale IQ, h^2 = 80-90%

   individual regions correlate much more with specific abilities

   performance IQ & prefrontal cortex volume genetic r = .72

   processing speed & white matter volume genetic r = .89

4. information-processing speed as measured by reaction time or working memory capacity

reaction time correlates - 0.2 → - 0.6 with IQ, h^2 = 54-58%

less more complex tasks

but only accounts for 10-30% of variance in IQ

Electro-physiological measures of brain function

EEG electroencephalography measures stimulus-evoked brain activity

α frequency (10 cycles/sec) most dominant freq. in human EEG
can be measured from various different brain regions

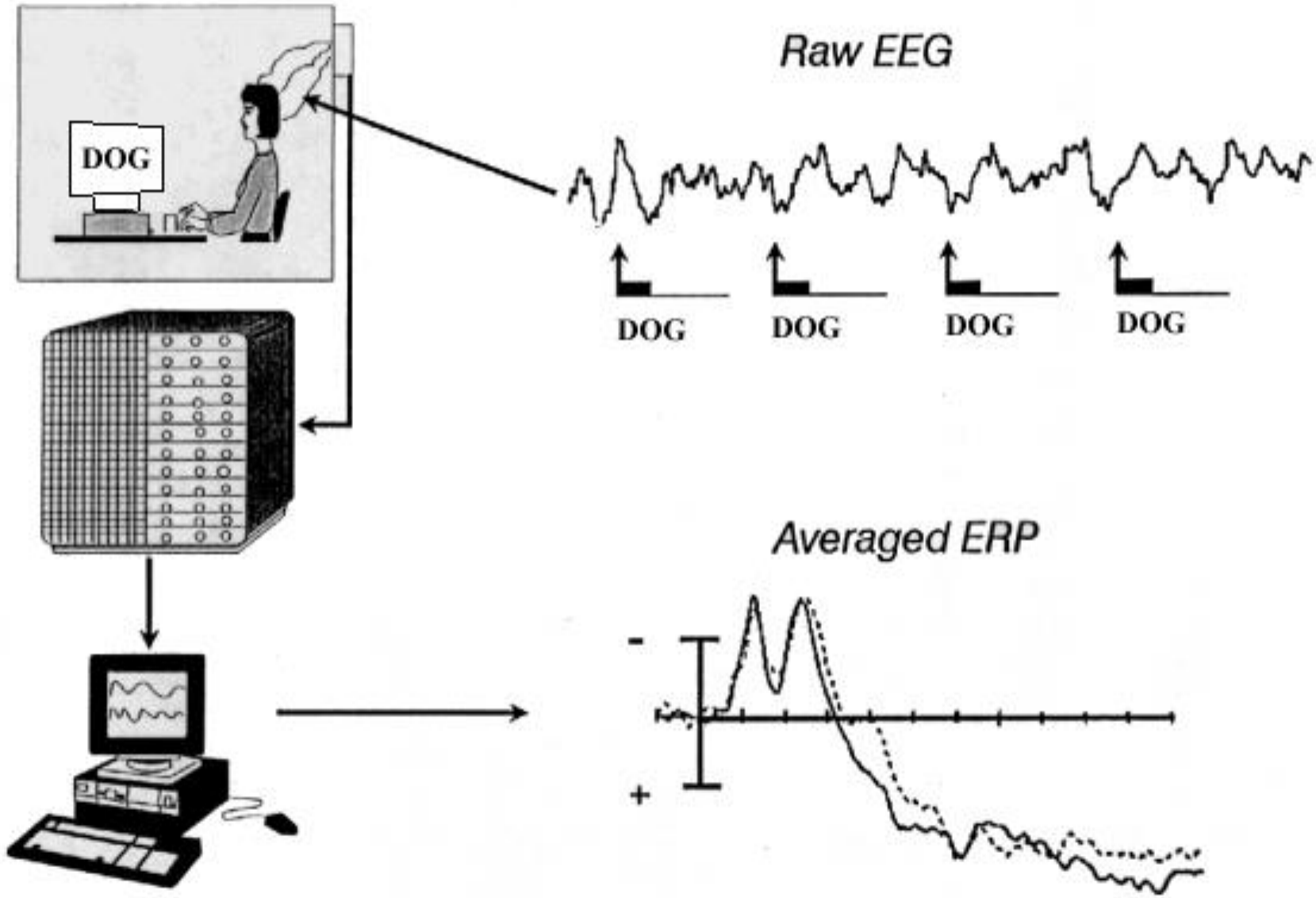
event-related potentials (ERPs) visual statistical analysis of EEG
α peak freq., verbal ability r = .35 components of ERP correlate more

Advantages
relatively low cost, non-invasive, large samples can be collected
provides direct real time measure of cortical neuronal activity
permits isolation of specific stages of processing

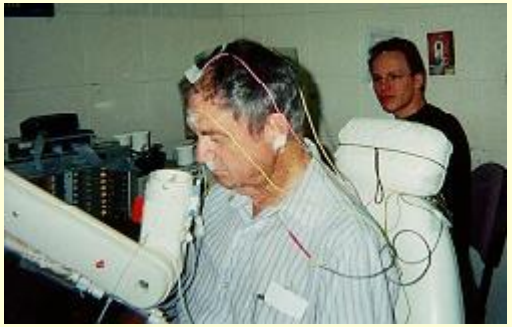
Disadvantages
very limited spatial resolution
sources cannot be precisely located

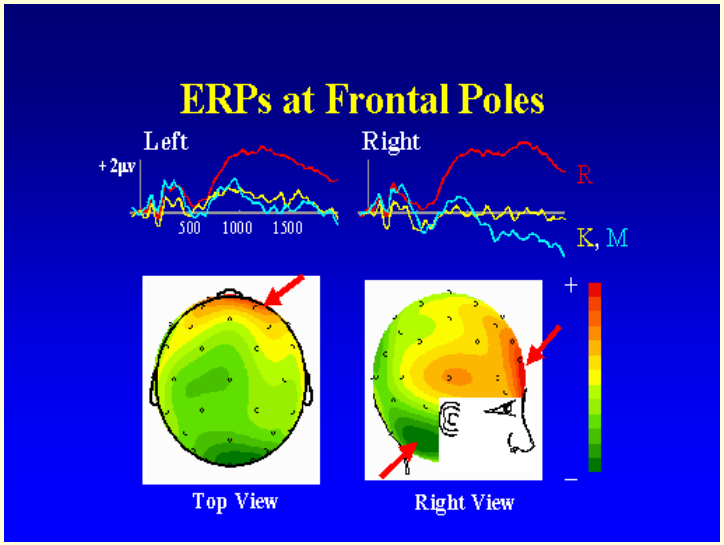
Combining with fMRI will help localize neural substrates of ERPs

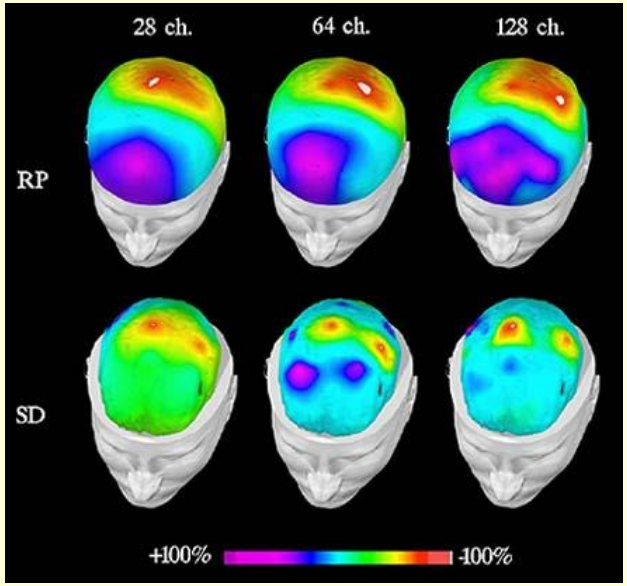
Event-Related Potential Technique



Event-related potentials





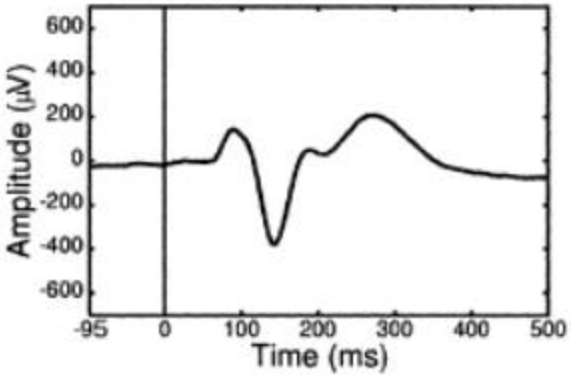


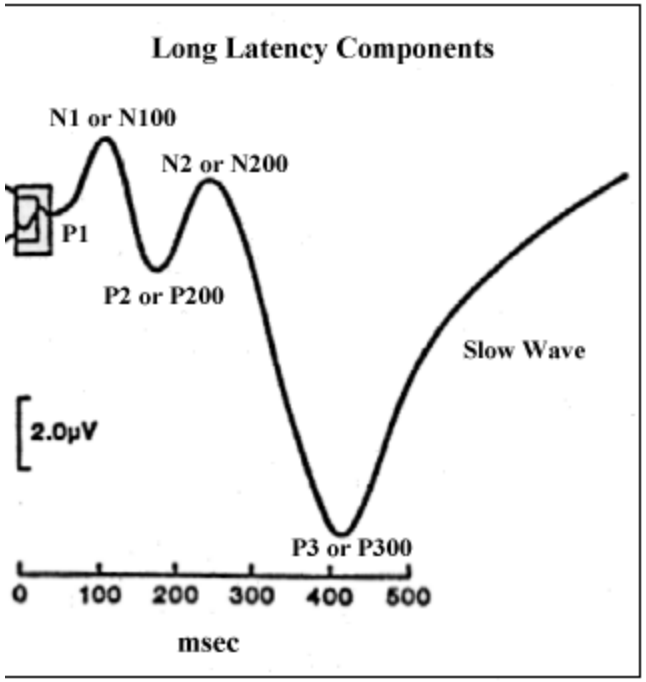
Example of ERP P300 (P3) brain potential

- can be used to measure cortical activity during stimulus discrimination tasks measure of attention and working memory
- large waveform, peaks (starting at ~ 300mS) after detection of attended & task-relevant stimulus

typical task: count infrequent relevant stimuli randomly appearing among irrelevant stimuli

- latency measures evaluation time
- amplitude gives measure of working memory resources allocated by brain





Used as endophenotypes for psychopathologies also

Identification of loci influencing cognition

whilst many gene **products** have been implicated in cognitive processes

few polymorphisms at gene loci have been consistently found to contribute to genetic variance for cognition

replicated linkage on 6p for reading ability

FNBP1L gene (formin-binding protein 1-like)– found in several studies – regulates neuronal morphology, expressed in neurons in developing brain

CTNNBL1 gene (beta-catenin-like protein 1)– memory-related – replicated in large GWAS

In past, most reported genetic associations with general intelligence were probably false positives (Chabris et al, Psy Sci. 2012)

Most Reported Genetic Associations with General Intelligence Are Probably False Positives

Christopher F. Chabris* [1]
Benjamin M. Hebert [2]
Daniel J. Benjamin [3]
Jonathan P. Beauchamp [2]
David Cesarini [4,5]
Matthijs J.H.M. van der Loos [6]
Magnus Johannesson [7]
Patrik K.E. Magnusson [8]
Paul Lichtenstein [8]
Craig S. Atwood [9,10]
Jeremy Freese [11]
Taissa S. Hauser [12]
Robert M. Hauser [12,13]
Nicholas A. Christakis [14,15]
David Laibson [2]

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3. Department of Economics, Cornell University
4. Department of Economics, New York University
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6. Erasmus School of Economics, Rotterdam
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Psychological Science, in press, last modified 5 December 2011

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miRNAs microRNAs

- ~21 nucleotides long, non-protein-coding
- guide effector protein Argonaute (AGO) to mRNAs of coding genes, most human mRNAs are regulated by miRNAs (how do mRNAs escape regulation? circRNAs?))
- repress protein production

Mouse model - complete miRNA-ome generated

488 miRNAs expressed in hippocampus

23 highly expressed (83% of total miRNA content)

some minimally expressed elsewhere – suggests special role in hippocampus

miRNA -34c especially associated w. learning

– impairs learning by interfering w. memory consolidation

- thought to silence SIRT1, gene product (the protein SIRTUIN 1) crucial for memory formation

- novel target for treatment for cognitive impairment

miRNA-34c inhibitors reversed impairment in mice overexpressing miRNA-34c

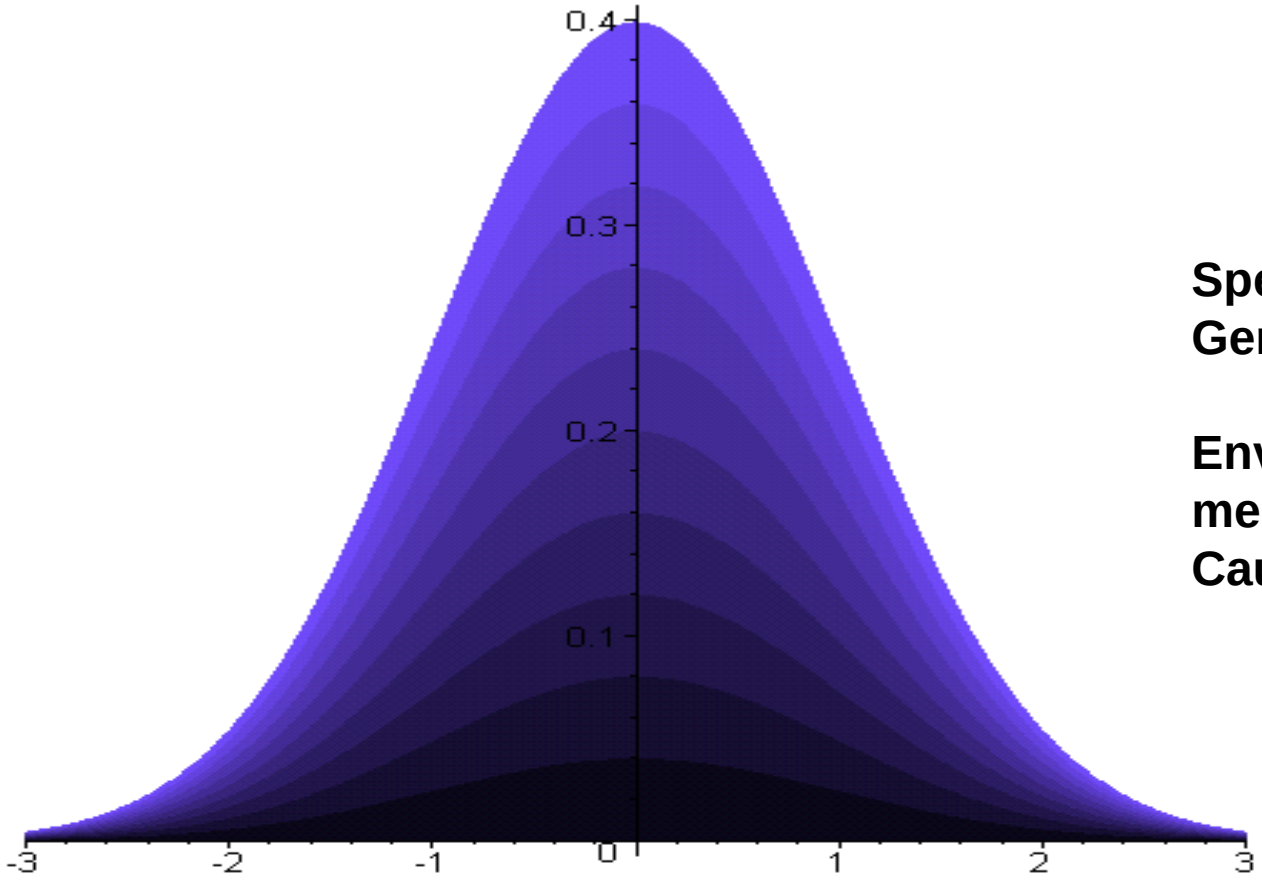
Also works in mouse Alzheimers model and aged mice (+2 years old)

Nature Reviews Neuroscience(2011),12 EMBO J (2011)

Will Flynn effect continue? Have we reached our maximum potential yet? Will people fall off bottom end of bell curve in our increasingly technological society?

Specific Genes

Environ mental causes



Specific Genes??

Environ mental Causes?

moderate severe profound Retardation

mild lower 1% <67

average

top 1% >137

IQs of 200 Genius