Psych 3102
Introduction to Behavior Genetics

Lecture 22

Childhood psychopathologies

(Developmental psychopathology)

Autistic disorder

- a mental disorder diagnosed within the first 3 years of life
- a severe neurodevelopmental disorder characterised by:

1.
2.
3.

typically no period of normal development

moderate retardation in 75% of cases IQ 35-50

more variable: hyperactivity, under- or over-sensitivity to sensory stimuli, impulsivity, aggression, self-injury

- only small % go on to live independently as adults

Commonly used screening tools:

Childhood Autism Rating Scale (CARS) - similar to DSMIV

Autism Behavioral Checklist (ABC) – does not exclude other developmental problems, gives false positive rate of 46%

Prevalence

autistic disorder: 3-6 in 10,000 (0.045%)
autism spectrum disorders: 1 in 300 (0.3%)

4 : 1 boys:girls

500% increase in diagnosed cases 1991-97

- increased awareness, changing diagnostic criteria, not new environmental causes

% phenocopies estimated to be very low

- originally thought to have environmental cause
  no reported cases of autistic children having autistic parents
  risk to siblings "only" 3 -10%

Twin and family studies

- all consistent, indicate strong genetic component
  first degree relative risk = 3 – 10%

Concordances

Relationship	Autistic disorder	Recent ✦ studies	Cognitive/social deficit
MZ twins	36%	70%	92%
DZ twins	0%	10%	10%
siblings	3%	10%	15%
unrelated	0.05%	0.05%	0.3%
		tetrachoric correlations	
MZ twins	0.91		0.99
DZ/sibs	0.44		0.55

✦ total population screening, systematic standardized methods of diagnosis, screening out of other conditions - ONLY idiopathic autism

Conclusions

- autism is almost completely genetically determined
- multivariate analysis: different genetic influences exist for the 3 types of symptoms (social, communications, restricted interests) + supported by cognitive and brain data [Happe, Ronald, Plomin, 2006]
- heritability 80 - 90%
- no evidence for shared environment
- very small non-shared environment component
- complex, quantitative inheritance –many genes, interactions
- any environmental factors likely work by interacting with susceptible genotypes

Known causes of autism spectrum disorders:

~5% have chromosomal anomaly (duplications of Angelman region, chr 15)

~10% have Mendelian condition (fragile X tuberous sclerosis)

85% have unknown genetic cause (idiopathic autism)

-several candidate DNA regions from whole genome scans chromosome 7q

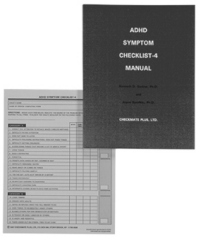
ADHD - attention-deficit hyperactivity disorder

Most predictive characteristics:

1.

2.

3.



DSMIII-R single category DSMIV 3 categories

ADHD I primarily inattentive

ADHD H/I primarily hyperactive/impulsive

ADHD C combined type

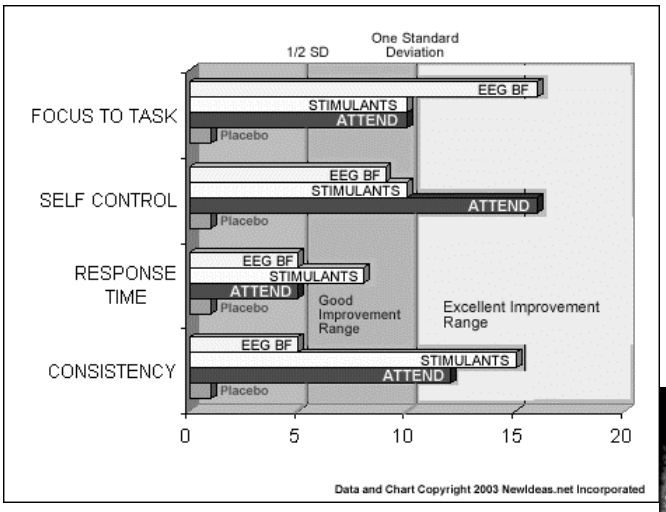
Prevalence: 6 - 7% at elementary school age

5 : 1 boys : girls

- continues into adolescence, 1/3 cases →adulthood
- frequently comorbid with CD, ODD
- increased risk for substance abuse, dependence

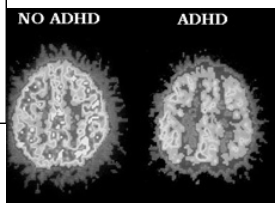
Problems

fake science or real?



over treatment?

what is this?



Family and adoption studies

Recent large US study: ADHD combined type

familial tendency: 25% first degree relative risk

5% prevalence

adoption studies: biological parent/offspring resemblance is much greater than adoptive parent/offspring

Twin studies

- consistent results even with different measurement methods and heterogeniety of phenotype

Concordances 20 twin studies

MZ = 51% DZ = 33% Prevalence = 5%

heritability ~ 76% no shared e

Using quantitative measure:

same sex, 13 year-old twins, hyperactivity ratings:

Rated by	Mother	Father	Teacher
MZ twins	0.68	0.48	0.62
DZ twins	-0.08	0.21	0.26

mother's ratings show contrast effects

genetic overlap between inattentive & hyperactive symptoms

Conclusions:

- clear genetic influence
- heritability ~70% range = 50 – 90% depending on measurement
- non-additive gene effects
- little evidence for shared environment

environmental risk factors identified in some studies: parental alcohol dependence, maternal smoking, maternal drinking during pregnancy, very low birth weight

mouse model: knock-out of dopamine transporter gene, chr 9

shows extreme hyperactivity

DRD4, DAT1 + other loci implicated in humans

Adolescent conduct disorder (CD)

- general disregard for rights & property of others
  - destruction of property, theft
  - aggressive behavior fighting, bullying
  - disobedience, lying, deceit, running away from home

Prevalence: 14 -20% boys > girls

CD is one of the most prevalent childhood disorders
most common reasons for psychiatric referral
strongest predictors of adult psychopathology

alcohol & drug dependence depression anxiety disorders
anti-social personality disorder

Latent trait analysis: ADHD/CD – genetic correlation with CD, differences produced by e

Older studies in text book

McGuffin (1985) juvenile delinquency

Twin concordances: MZ = 87% DZ = 72%

Twin correlations for quantitative measures:

	CBCL by mother	Rutter scale by mother
MZ boys	0.47	0.73
girls	0.56	0.70
DZ boys	0.40	0.50
girls	0.38	0.55
opposite sex	0.49	0.32

- modest/low genetic influence, heritability higher in girls
- sex differences for Rutter scale ratings
- large non-shared and shared environment
  - CBCL Childhood Behavioral Checklist

Problems identified in study methodology:

- sample ascertainment
- age distribution
- method of assessment

- Heterogeneity

Large environmental component - role of family emphasized

- ineffective and/or harsh parenting, poor supervision, lack of discipline, parental conflict, separation, divorce
- all identified as risk factors for CD

- but could these reflect parental psychopathology?

Recent studies

example: Slutske et al (1997) J. Abnormal Psych

2682 twin pairs community-based sample DSMIII-R

Australian Twin Registry Male prevalence = 20%

Female prevalence = 3%

		n	Concordance	Tetrachoric r
Male	MZ	396	0.53	0.70
	DZ	231	0.37	0.37
Female	MZ	930	0.30	0.68
	DZ	533	0.18	0.48
Opposite sex		592		0.34
- male proband			0.08	
- female proband			0.45	

- larger genetic influence
- shared environment < 30%
- sex differences in prevalence rates but not influences

Peer influence

- previously identified as part of environmental influence
- but,

Genes for 'bad behavior'?

- mediation of gene influence is likely to be via personality attributes, cognitive style

Comorbidity with ADHD

CD probands 30-50% also have ADHD

ADHD probands 50% show CD/antisocial symptoms

latent trait analysis – type of multivariate analysis capable of revealing underlying influences , here = genetic influence

DRD4 7-repeat(long) allele associated with ADHD and comorbid CD