

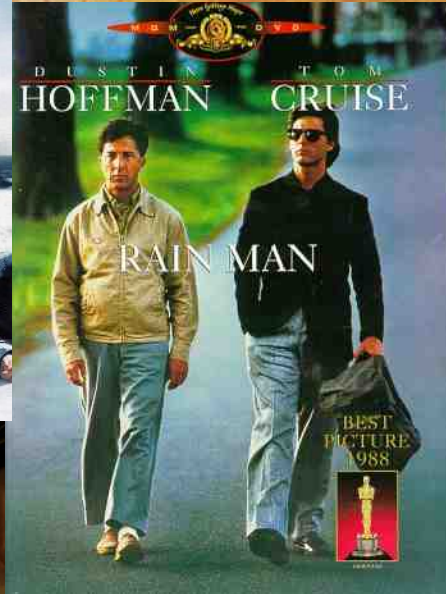
# **Applications in Psychology**

## **Examples of behaviour genetic research on autism spectrum disorders**

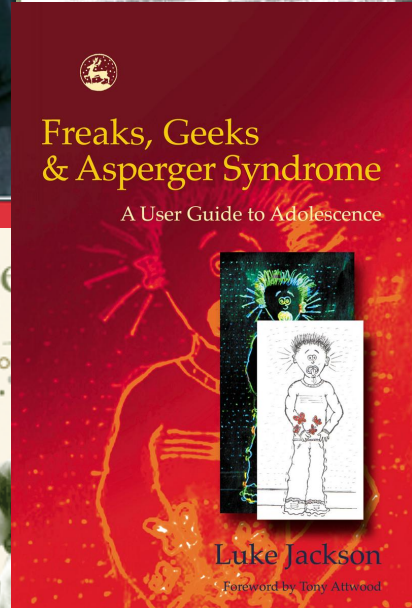
Dr Angelica Ronald,  
Genes Environment Lifespan laboratory,  
Birkbeck

5<sup>th</sup> April 2013

Genetics for Social Scientists, LSHTM



# Autism



# Outline

- What is autism today and what causes it?
- Why does autism co-occur with other conditions? (comorbidity)
- Is there a single explanation for autism? (multivariate analyses)
- Have we found the genes?
- What role does the environment play?

# What is autism today?

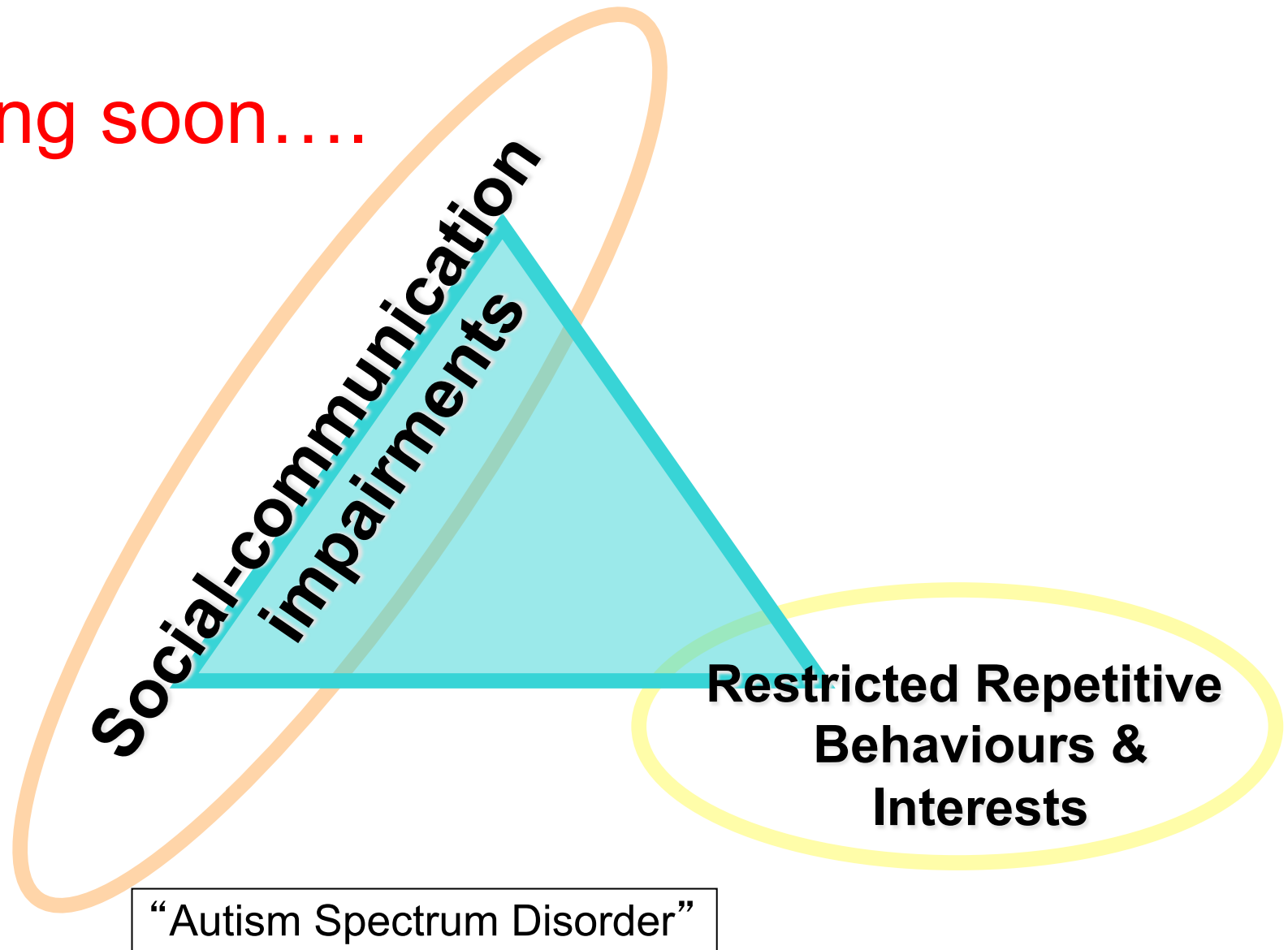
**Social  
impairments**

**Communication  
impairments/  
language delay**

**Restricted Repetitive  
Behaviours &  
Interests**

Autistic disorder  
Aspergers disorder  
Pervasive developmental disorder not otherwise specified (PDD  
NOS)

Coming soon.....



See [www.dsm5.org](http://www.dsm5.org) for forthcoming revisions

# What causes autism?

# What causes autism

## Ideas from pre-1968:-

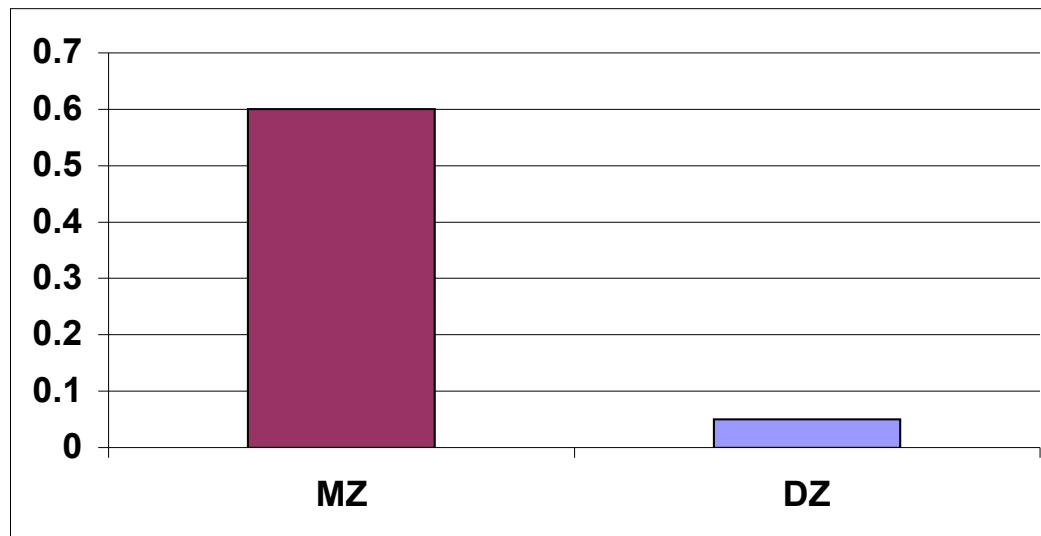
- Type of mental subnormality
- Childhood schizophrenia
- Genetic basis
- Psychogenic explanation e.g. cold parenting
- Social withdrawal
- Brain damage
- Abnormality of physical arousal
- Language impairment



# Family studies demonstrated that autism is familial

- Sibling risk (3-4%) vs. Population rate (0.1-0.6%) (Rutter 1968)
- Relatives show autistic traits (Bolton et al., 1994)

# Twin studies demonstrated that autism is highly heritable



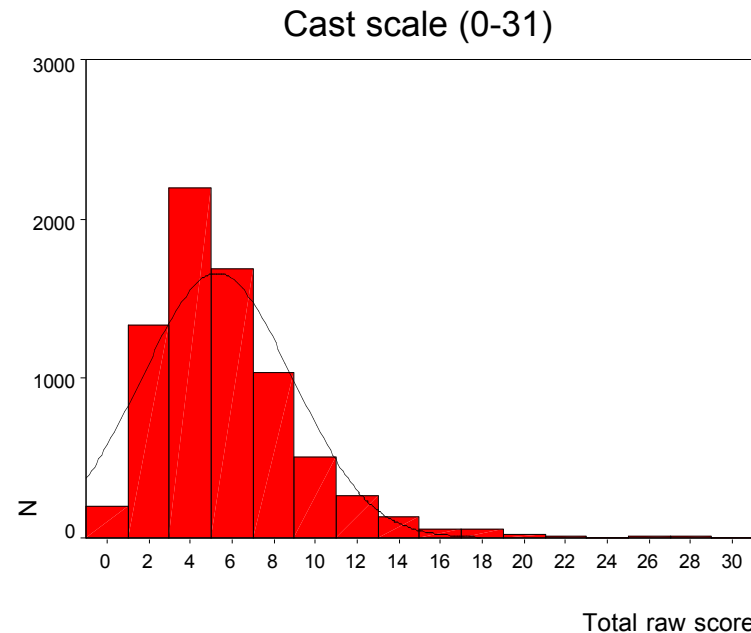
MZ = Monozygotic twins

DZ = Dizygotic twins

Ronald & Hoekstra (2011) Autism Spectrum Disorders and Autistic Traits: A Decade of New Twin Studies. *Neuropsychiatric Genetics*

# Heritability of autistic traits

- Using extremes analyses, twin studies have shown that heritability does not change across the distribution of autistic traits



Ronald et al (2006) *Journal of the American Academy of Child and Adolescent Psychiatry*

Robinson et al (2011) *Archives of General Psychiatry*

Lundstrom et al (2012) *Archives of General Psychiatry*

# Outline

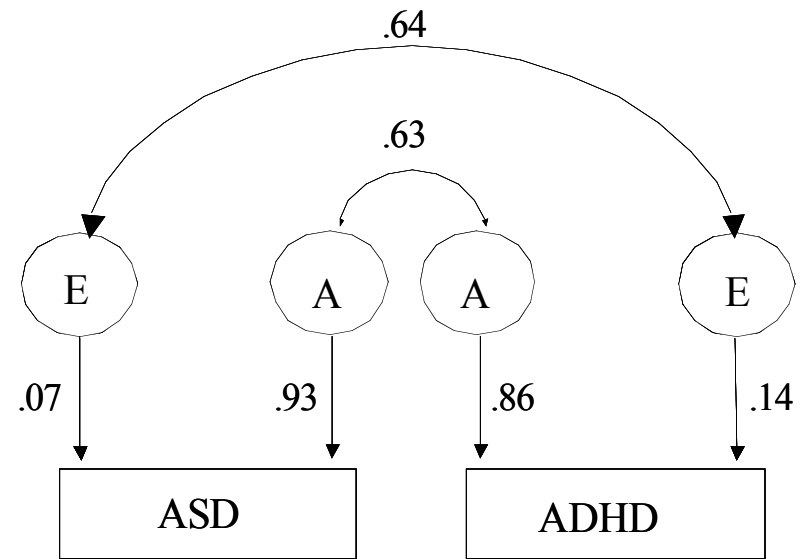
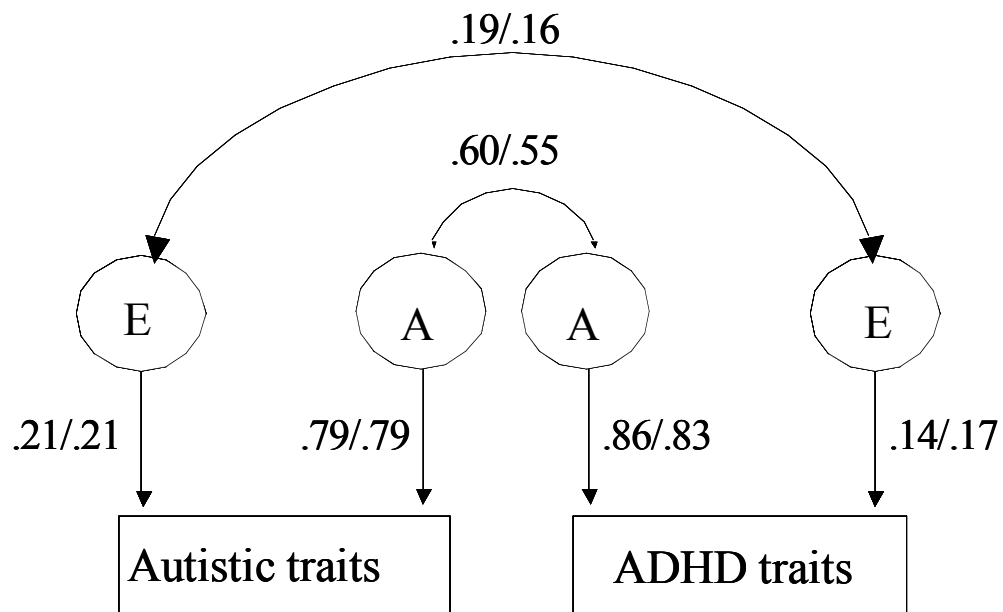
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Why does autism co-  
occur with other  
conditions?  
(comorbidity)

# Substantial genetic overlap between autism and attention deficit hyperactivity disorder (ADHD)

Traits in the population

Categorical diagnoses



Male/female

# ASD + ADHD: Why?

- Family studies -- shared familial influences  
(Mulligan et al., 2008; Nijmeijer et al., 2009)
- Twin studies -- overlapping genetic and environmental influences (Constantino et al., 2003; Reiersen et al., 2008; Ronald et al., 2008, Ronald et al., 2010; Lundstrom et al., 2011; Taylor et al., in press)
- Common genes implicated e.g., dopamine and serotonin-related polymorphisms (For a review see: Rommelse et al., 2010 *Eur Child Adolesc Psychiatry*; Neale et al., 2010 *JAACAP*)

# Outline

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Is there a single  
explanation for autism?  
(multivariate analyses)

$r_{ph}$  = phenotypic correlation

$r_g$  = genetic correlation



**Social**

$r_{ph} = ?$

$r_g = ?$

$r_{ph} = ?$

$r_g = ?$



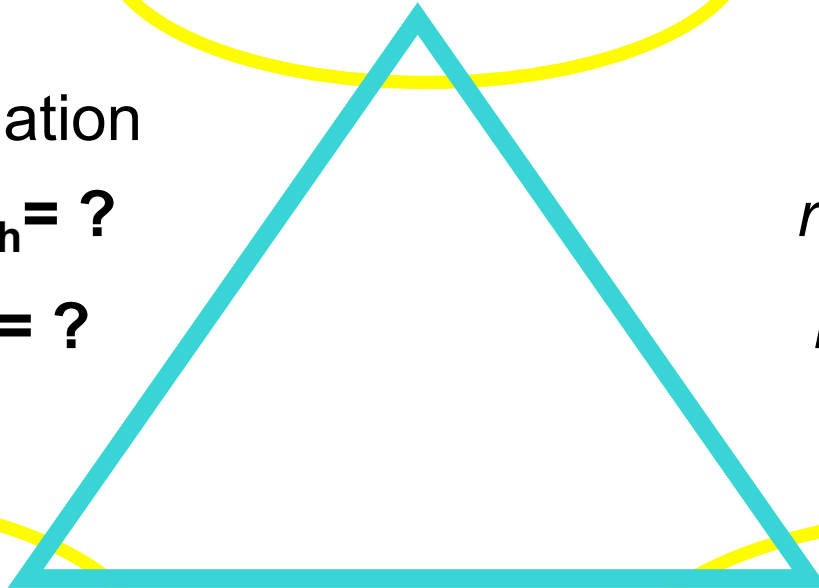
**Communication**

$r_{ph} = ?$

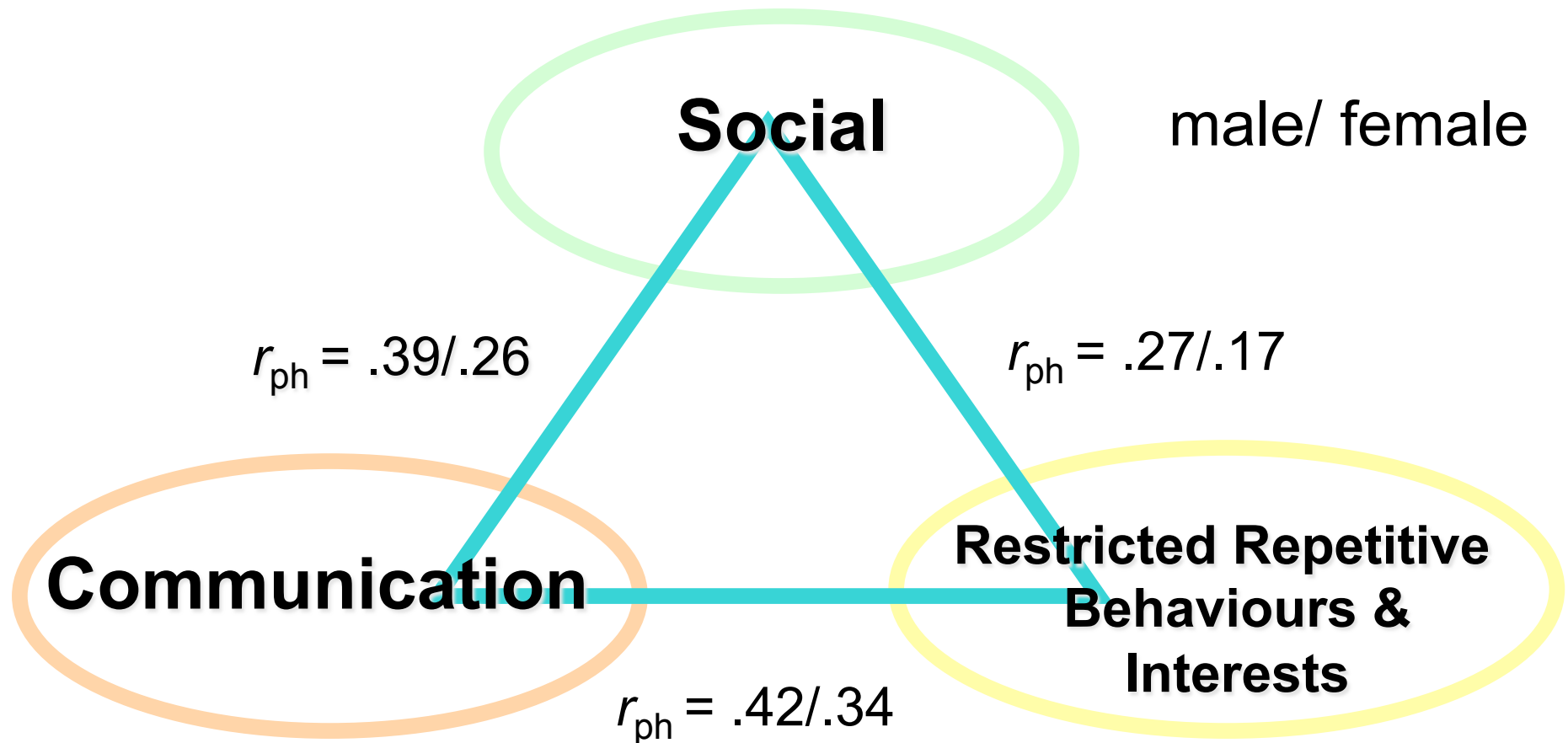
$r_g = ?$



**Restricted Repetitive Behaviours & Interests**

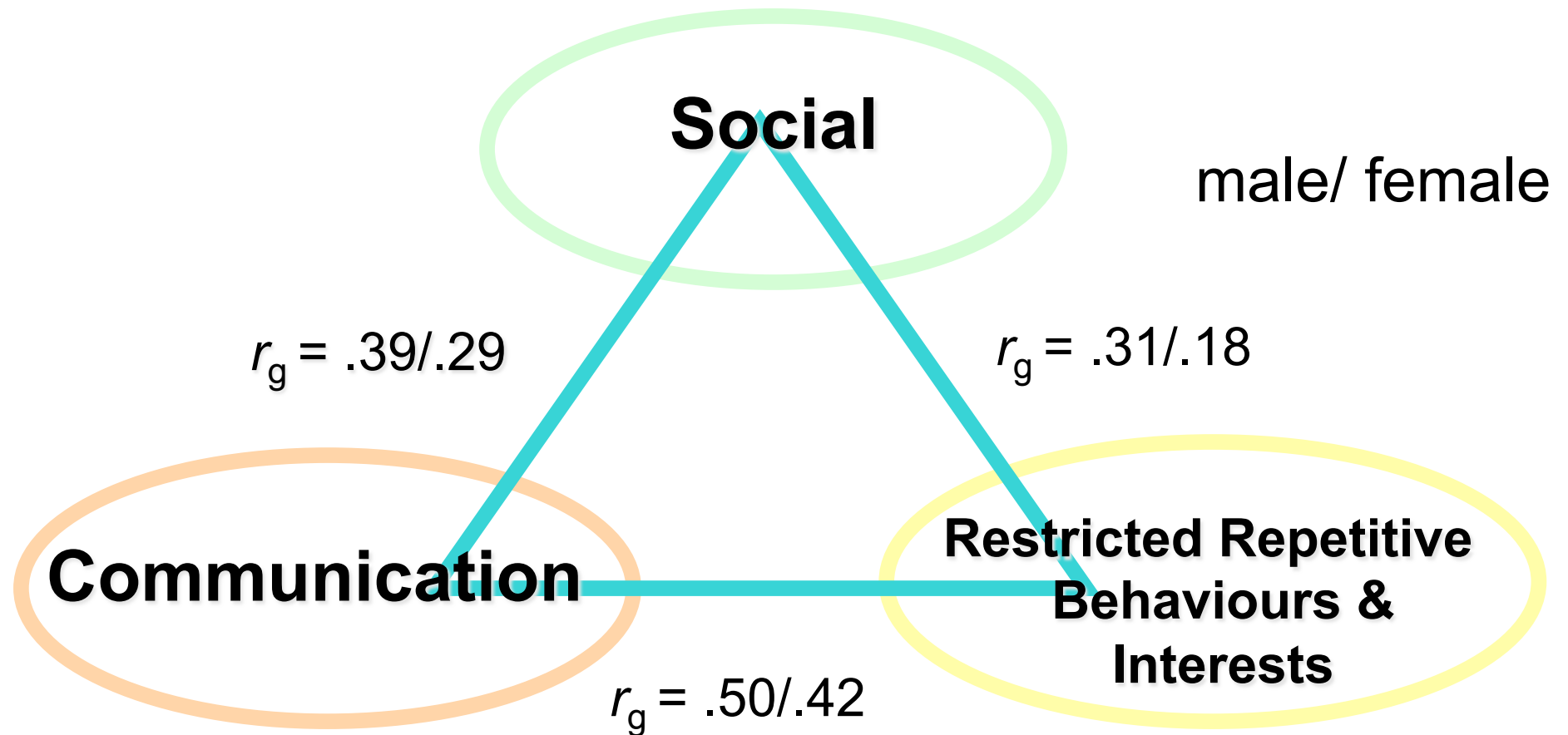


# Weak links between autistic-like traits in the general population



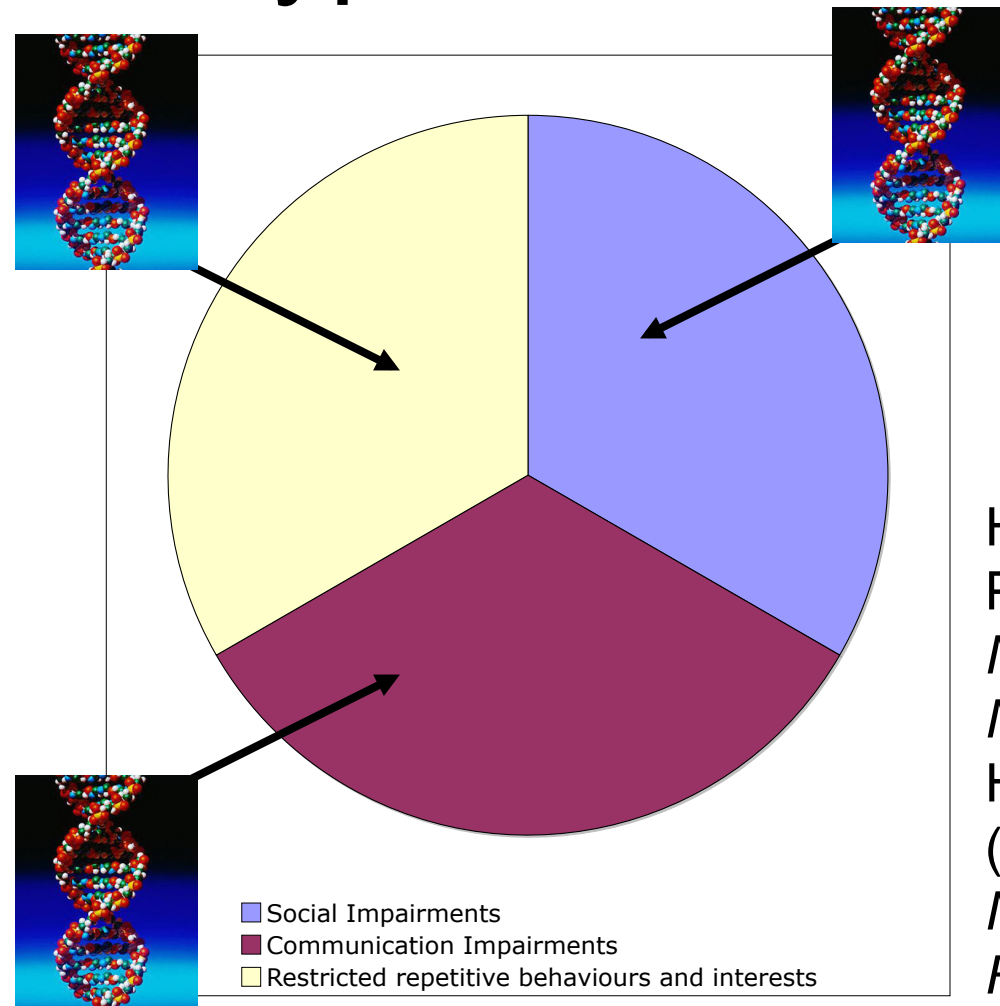
Ronald, et al (2006) *Journal of the American Academy of Child & Adolescent Psychiatry*  
See also: Ronald, et al (2010) *Molecular Psychiatry*; Robinson et al (2012) *Behavior Genetics*

# Modest genetic overlap between different autistic-like traits at age 8



Ronald et al (2006a) *Journal of the American Academy of Child & Adolescent Psychiatry*  
See also: Ronald, et al (2010) *Molecular Psychiatry*; Robinson et al (2012) *Behavior Genetics*

# Fractionable autism triad hypothesis



Happé, Ronald &  
Plomin (2006)  
*Nature  
Neuroscience*;  
Happé & Ronald  
(2008)  
*Neuropsychology  
Review* 21

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Have we found the  
genes?

# Familial & Syndromic Autistic Spectrum Disorders

## Syndromic

- *Known* biological cause
- Make up **10-20%** of all ASD cases
- 3 types:
  - 1). Genetic syndromes with comorbid ASD (1-2% cases)
  - 2). Cytogenetic lesions (6-7% of cases)
  - 3). De Novo copy number variations (~2-10% of cases)

## Familial

- Cause(s) unknown
- 80-90% of cases
- Autistic traits elevated in families of children with familial ASD (the '*broader autism phenotype*')
- Multiplex families

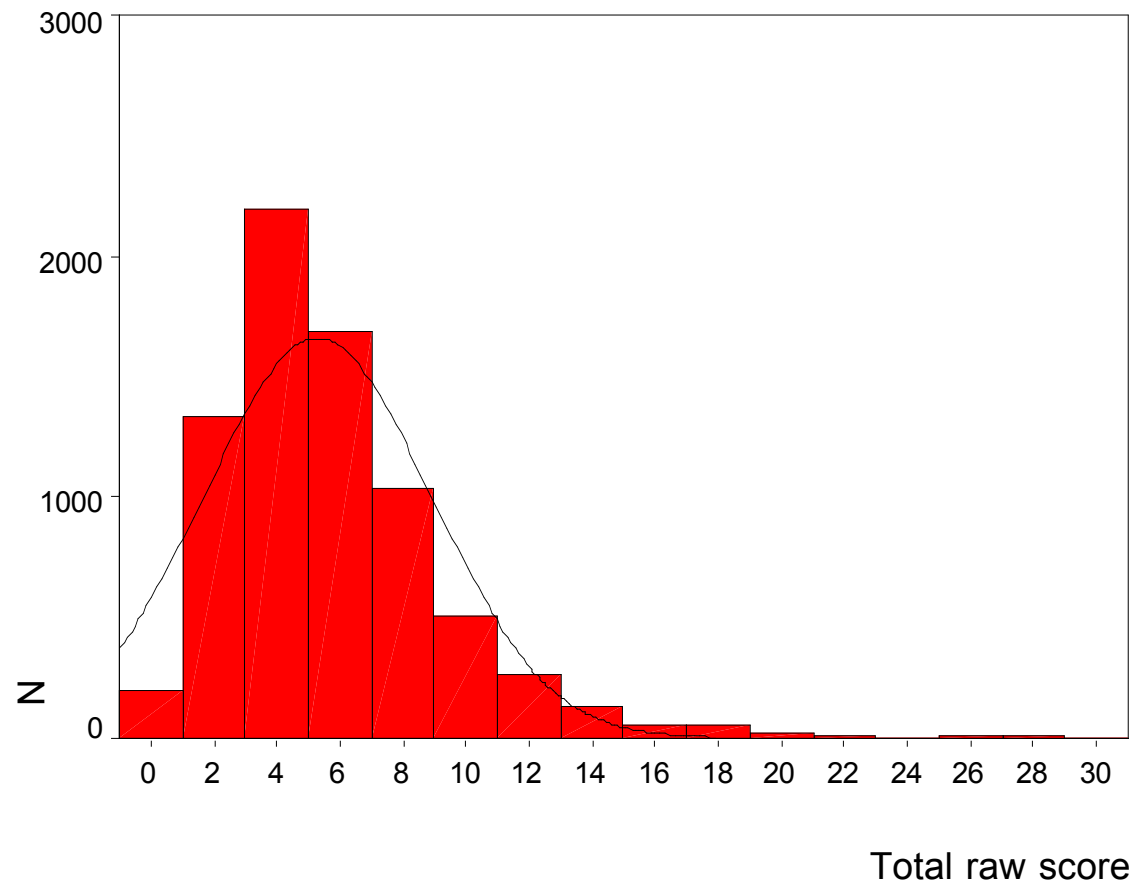


# Challenges to autism genetic research

- Power to detect small genetic effects
- Reliability -- and variety -- of diagnoses
- Variation in causal pathways within samples
- Psychiatric comorbidity
- Control group contamination

# Autistic traits

Cast scale (0-31)



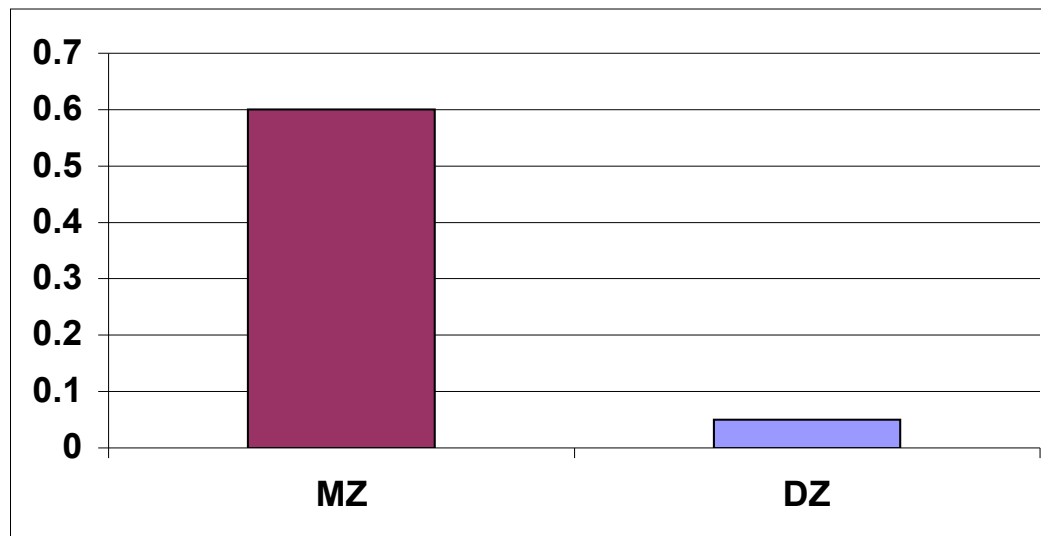
CAST = Childhood Asperger Syndrome Test

# Common genetic variants associated with autistic traits

Study	Sample	Result	Chromosome
Ronald et al (2010) <i>Behavior Genetics</i>	TEDS and AGRE	rs11894053 intergenic (nominal significance)	2p21
St Pourcain et al (2010) <i>American Journal of Psychiatry</i>	ALSPAC	rs4307059 intergenic	5p14.1
Steer et al (2010) <i>PLOS One</i>	ALSPAC	rs4307059 intergenic & 3 SNPs in CNTNAP2 gene	5p14.1 and 7q35

What role does the environment play?

# Twin studies of autism



MZ = Monozygotic  
twins

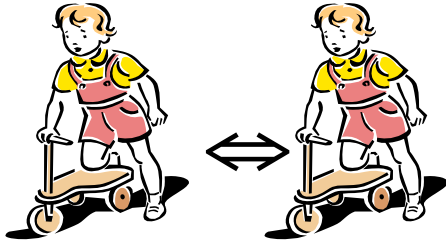
DZ = Dizygotic  
twins

Ronald & Hoekstra (2011) Autism Spectrum Disorders and Autistic Traits:  
A Decade of New Twin Studies. *Neuropsychiatric Genetics*

# Autism and Birth Complications

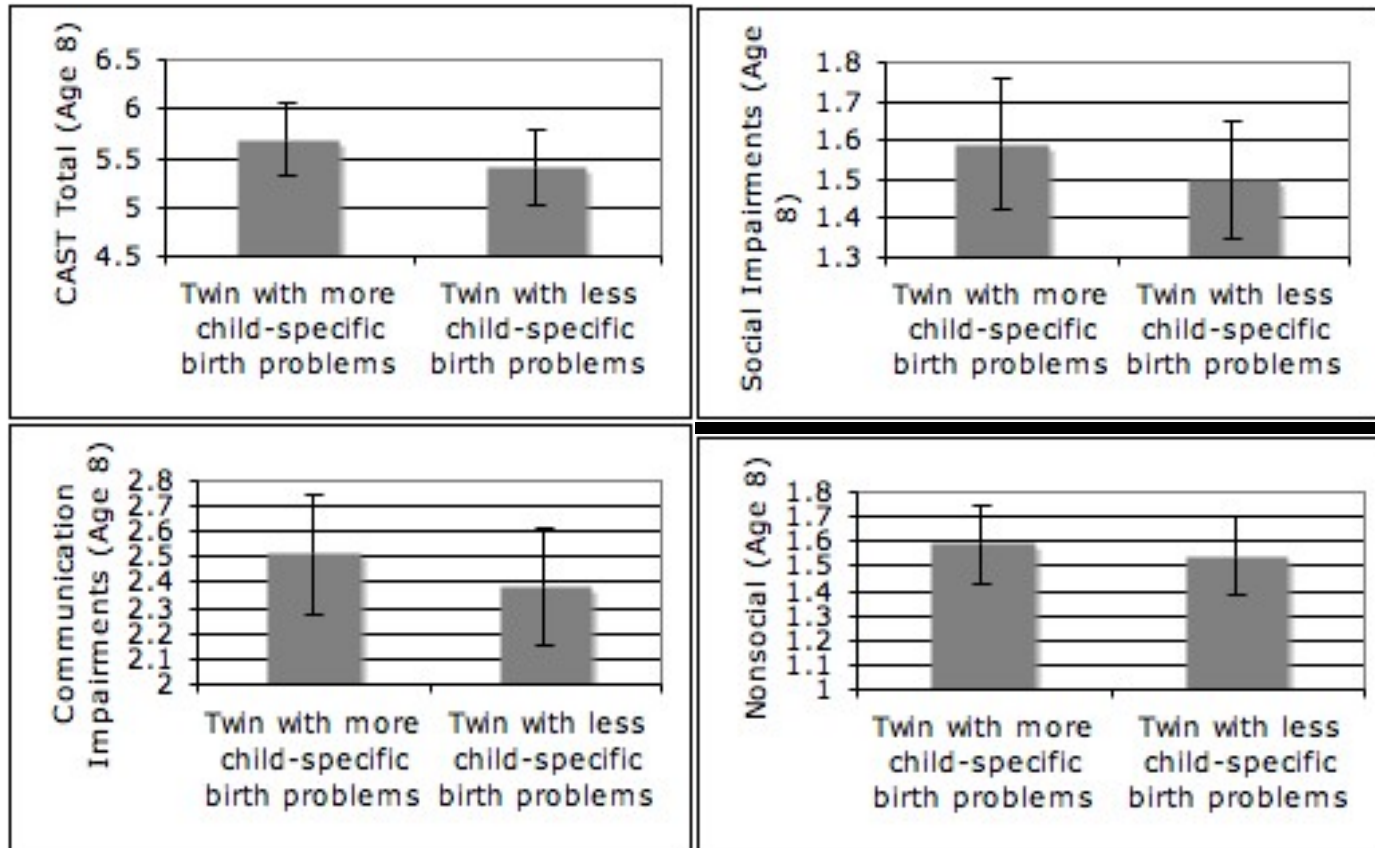


*Cause or  
Consequence?*



# Differences within MZ pairs discordant for birth problems

From Ronald et al (2010) *Child Development*



N = 63 pairs

# Differences in identical twins





# Conclusions

- Autism is an umbrella term for a wide spectrum of behaviourally-defined conditions
- Genetic research is advancing, but still much remains unknown
- Environmental research mainly focuses on prenatal, perinatal and postnatal complications

# Conclusions

- Behaviour genetic research has greatly advanced our understanding of autism since the 1960s
- Behaviour genetic evidence suggests both genes and environment play a role in causing autism spectrum disorders
- Recent twin studies show that there is not a clear etiological distinction between extreme autistic traits and milder autistic traits

# Conclusions (cont.)

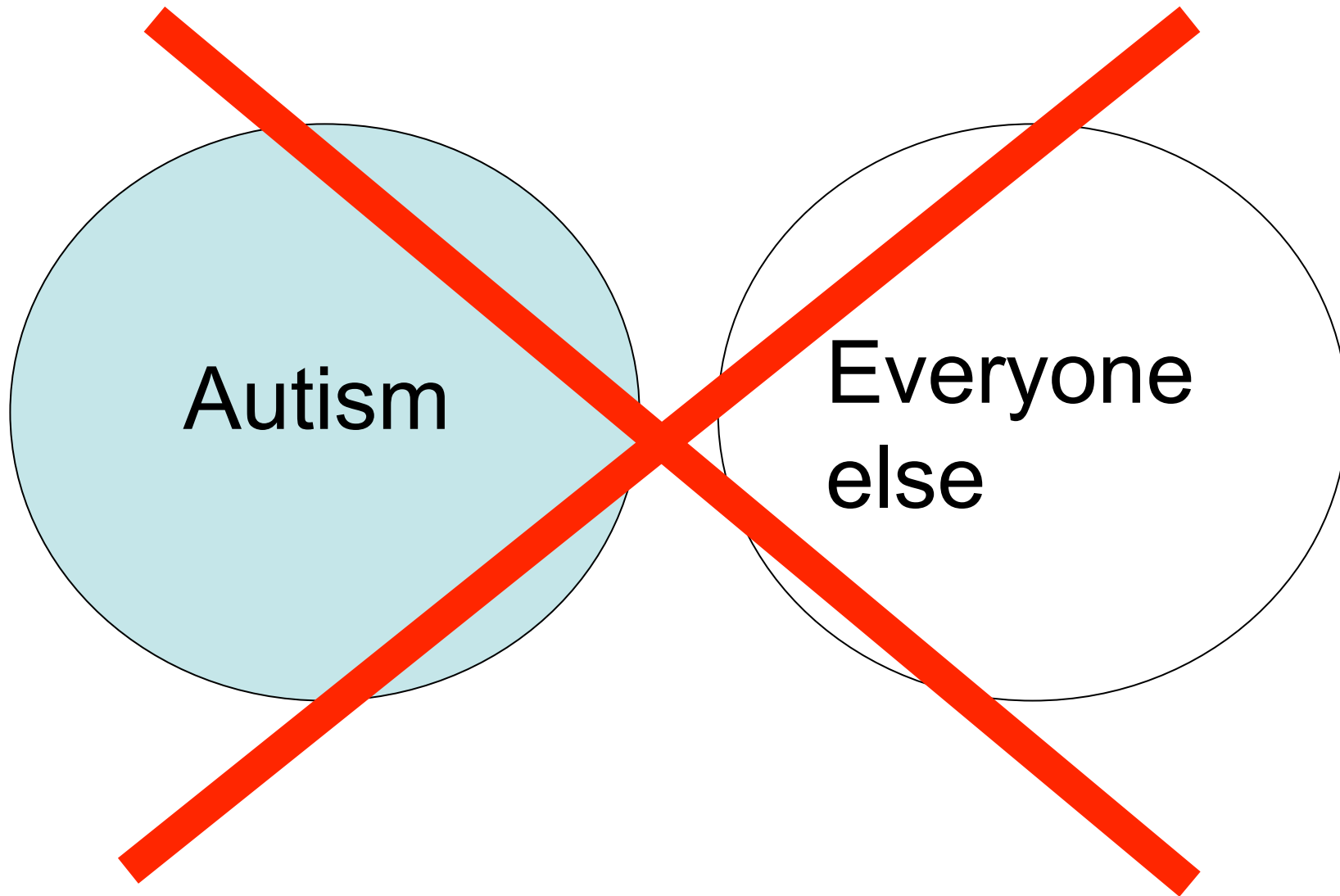
- Twin and family studies have demonstrated why other conditions, such as ADHD, co-occur with autism and autistic traits
- Twin studies have revealed that different symptoms within autism spectrum disorders appear to have largely different genetic and environmental causes



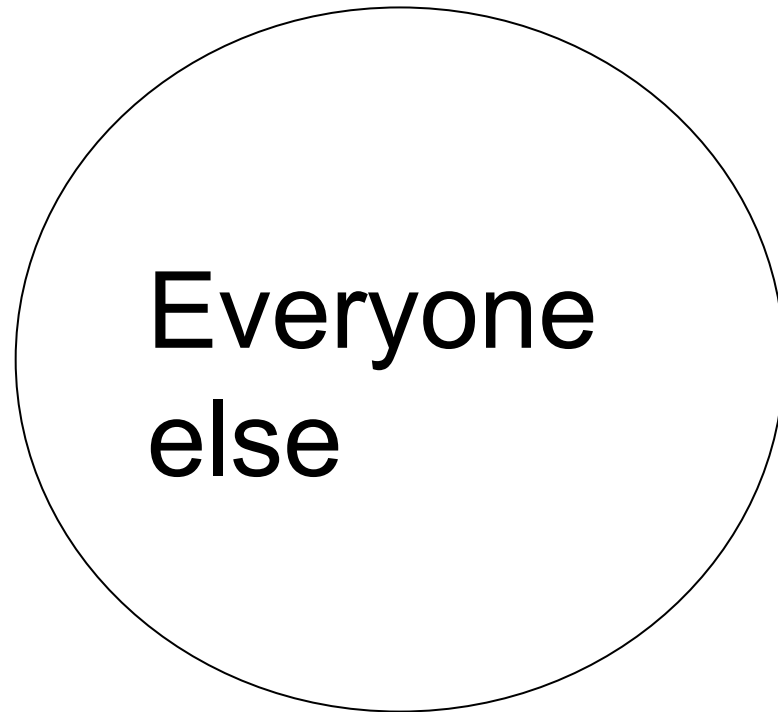
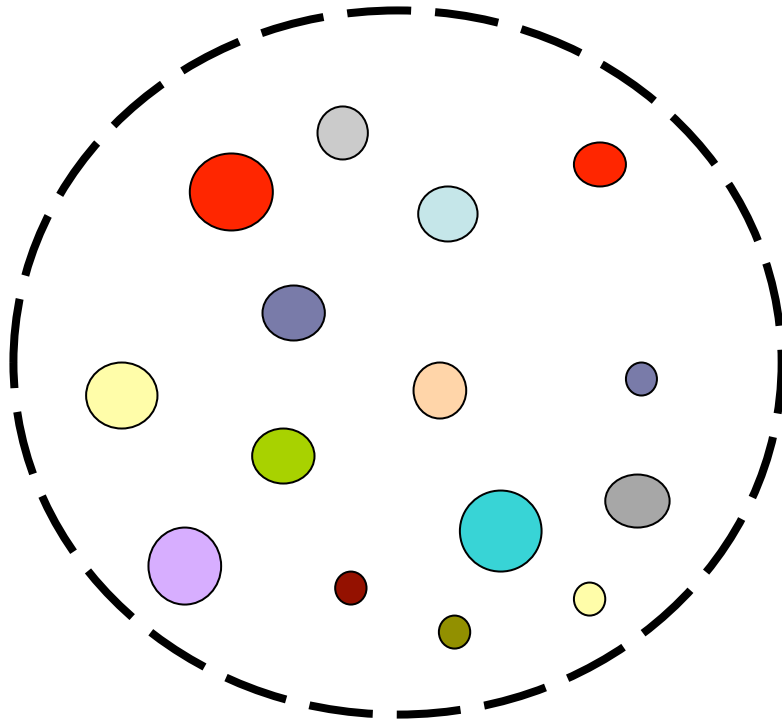
**Autism**



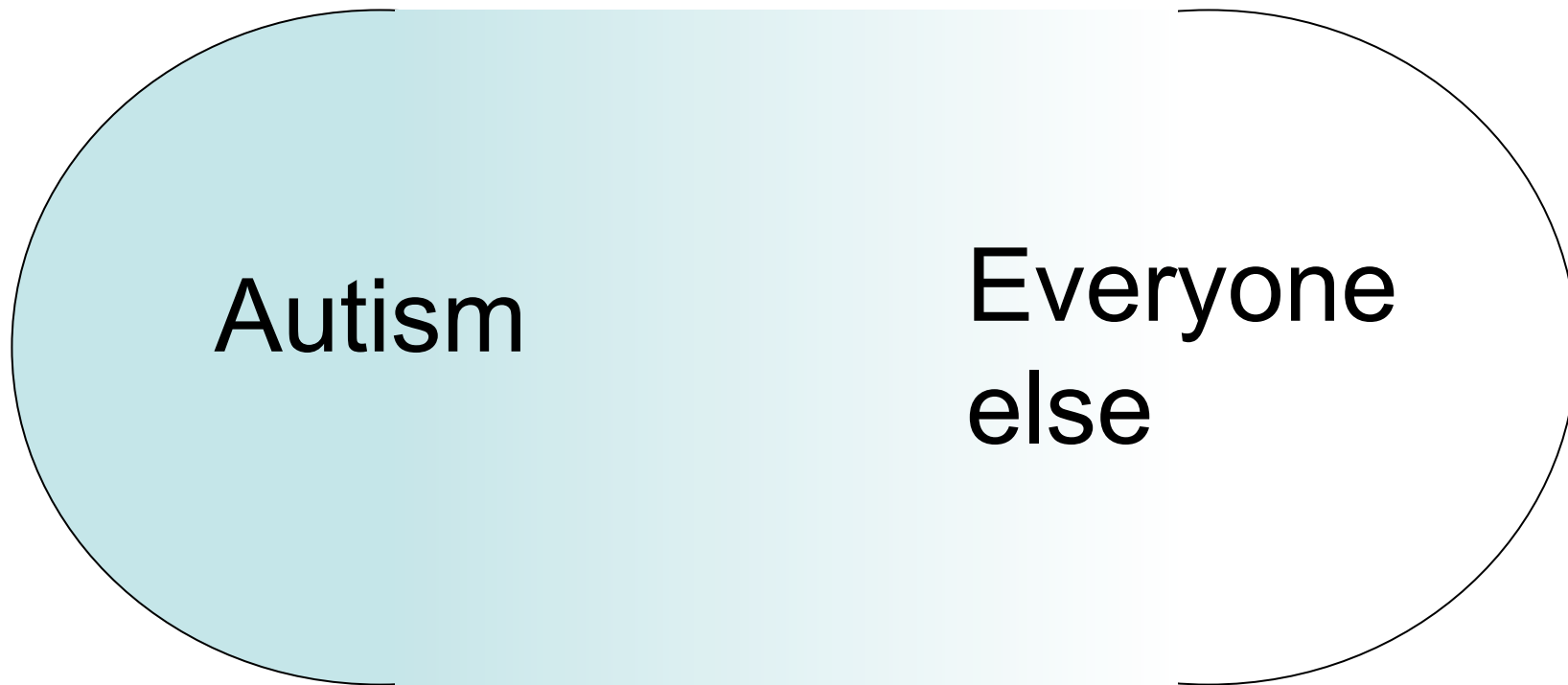
**Everyone  
else**



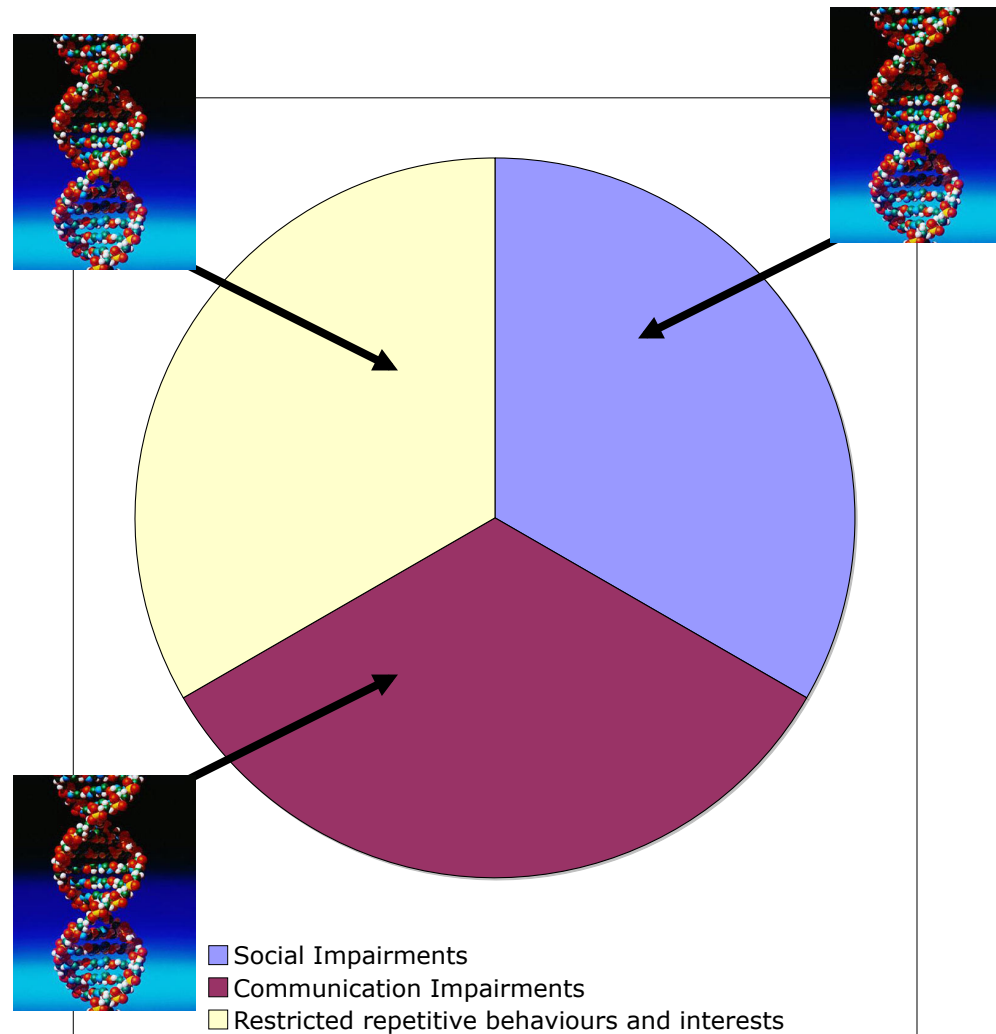
## ***Reason 1. “The Autisms”***



***Reason 2. Lack of clear boundaries between autism and typical variation***



# ***Reason 3. Multiple symptoms with partly different causes***





# Learning Questions

- Before family and twin studies, what did people think caused autism?
- What causes the comorbidity between ADHD and autistic traits?
- Can autism be explained by a single set of genes?
- What does the fractionable autism triad hypothesis propose?
- What type of environmental influences may play a role in influencing risk for autism and autistic traits?