The nature and nurture of ADHD – a developmental perspective

Corina Greven, PhD
Overview

1. Introduction to the nature-nurture debate
2. The nature and nurture of ADHD
3. Developmental aspects
4. Nature-nurture misunderstandings
% who think nature (genes) is at least as important as nurture (environments)

- Beh. Problems
- Personality
- Learning difficulties
- Mental illness
- Intelligence

Teacher (N=667)  Parent (N=1340)

Walker & Plomin, 2005
Nature – nurture controversy

• One of oldest debates

• Until 1960s: View in favour of nurture dominated (e.g. schizophrenogenic mother)

• Now: Not genes versus environments
  genes and environments!

• How do we know?
Quantitative genetics

- Estimates heritability.
- As much study of genes as of environments.

Quantitative Genetic Research Designs

- Family Design
  - First degree relatives
  - Larger family pedigrees

- Adoption Design
  - Adoptive vs. non-adoptive relatives
  - e.g.,

- Twin Design
  - Mono- vs. dizygotic twins
  - Twins apart and together
  - e.g.,

- IVF Design
  - Parents who differ in genetic relatedness
  - e.g.,
Twin studies

Monozygotic (MZ)

Genetic similarity = 100%

Dizygotic (DZ)

Genetic similarity = 50%

• *Logic*: If MZ more similar than DZ twins $\rightarrow$ trait must be genetically influenced (= heritable)
Twin studies

• Estimate the contribution of genetic and environmental factors to individual differences (variance) in a trait.

• We typically estimate:
  • Additive genetics (heritability)
    - MZ 100%
    - DZ 50%
  • Common (shared) environment
    - MZ 100%
    - DZ 100%
  • Environment specific to each twin (non-shared)
    - MZ 0%
    - DZ 0%

• Shared or non-shared?
  • Divorce? Shared classroom environment/ shared teacher?
  • Differential effects of: accidents, perceptions of environment, physical illness
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Twin studies on ADHD

• High heritability of ADHD [1].

• Little evidence for aetiological gender differences [2].

• 2 dimensions: INATT and HYP-IMP [3-4].

## Twin studies: other child behavioural problems

<table>
<thead>
<tr>
<th>Trait/disorder</th>
<th>Heritability (A)</th>
<th>Shared environment (C)</th>
<th>Non-shared environment (E)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>70%</td>
<td>0%</td>
<td>30%</td>
</tr>
<tr>
<td>Oppositional defiant problems</td>
<td>59%</td>
<td>10%</td>
<td>31%</td>
</tr>
<tr>
<td>Conduct problems</td>
<td>58%</td>
<td>15%</td>
<td>28%</td>
</tr>
<tr>
<td>Depression</td>
<td>44%</td>
<td>14%</td>
<td>42%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>48%</td>
<td>12%</td>
<td>40%</td>
</tr>
</tbody>
</table>

Meta-analysis: Burt 2009 Psychol Bull
Twin studies on ADHD: rater effects

• Modest rater agreement [1].

• Heritability **parent** > **teacher** > **child**-report [2]. → same vs different rater?

• Most (~80%) of association between raters explained by shared genes [2].

What genes explain the heritability of ADHD?

- Individual genes cannot explain high heritability of ADHD

The case of the missing heritability

Maher 2008 Nature
SNP heritability

• SNP = single nucleotide polymorphism

SNP HERITABILITY

Genetic similarity

SNP similarity of unrelated individuals

↓

Behavioural similarity

If individuals who are more similar genetically, are also more similar behaviourally → trait is heritable

• All SNPs in the genome together. No specific genes.
SNP heritability

- 4100 individuals with ADHD
- 12000 controls

• Explain almost half of twin heritability using DNA.

Psychiatric Genomics Consortium 2013 Nature Genetics
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Heritability of ADHD over time


Genetic contributions to developmental course

Greven 2011 J Abnorm Psychol.
Gene contributions to developmental course

- > 8300 twin pairs, population-based.
- Genes explained 80% of individual differences in change of HYP-IMP.
- Different genes involved in risk for HYP-IMP in childhood, and developmental course into late adolescence.

→ Helps explain why some children with ADHD remit, others persist.

Pingault Viding Galera Greven 2015 JAMA Psychiatry
Is Adult ADHD a Childhood-Onset Neurodevelopmental Disorder? Evidence From a Four-Decade Longitudinal Cohort Study

Terrie E. Moffitt, Ph.D., Renate Houts, Ph.D., Philip Asherson, M.D., Maggie Hammerle, B.A., HonaLee Harrington, B.A., Sean F. Dick, M.D., Guilherme V. Polanczyk, M.D., Richie Poulton, Ph.D., Sandhya Kumar, M.D., Luis Augusto Rohde, M.D., Avshalom Caspi, Ph.D.

- 90% of adults lacked childhood diagnosis of ADHD.
- May reflect different genes than childhood ADHD.

Evaluation of the Persistence, Remission, and Emergence of Attention-Deficit/Hyperactivity Disorder in Young Adulthood

Jessica C. Agnew-Blais, ScD; Guilherme V. Polanczyk, MD, PhD; Andrea Danese, MD, PhD; Jasmin Wertz, MSc; Terrie E. Moffitt, PhD; Louise Arseneault, PhD

Attention-Deficit/Hyperactivity Disorder Trajectories From Childhood to Young Adulthood
Evidence From a Birth Cohort Supporting a Late-onset Syndrome

Arthur Caye; Thiago Botter-Maio Rocha, MD, MSc; Luciana Anselmi, PhD; Joseph Murray, PhD; Ana M. B. Menezes, PhD; Fernando C. Barros, PhD; Helen Gonçalves, PhD; Fernando Wehrmeister, PhD; Christina M. Jensen, MSc; Hans-Christoph Steinhausen, MD, PhD, DMSc; James M. Swanson, PhD; Christian Kieling, MD, PhD; Luis Augusto Rohde, MD, PhD
Why late-onset ADHD?

• Disorder may be masked in childhood? (protective factors)

• ADHD-like symptoms caused by another disorder?

• A distinct disorder? (lower heritability, more women)
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Nature–nurture misunderstandings: right or wrong?

1. If genetics is important for ADHD, there is nothing you can do about it.

2. Heritability of ADHD is 70%. This means the disorder has genetic origins in 70% of individuals with ADHD.

3. Low estimates of shared environmental influences on ADHD mean that parenting does not matter.
Nature–nurture misunderstandings (1)

If genetics is important, there is nothing you can do about it. (Wrong!)

- Genes are **risk factors**, not destiny
  - **Weight** (diet), **phenylketonuria** (diet), **ADHD** (medication, parent management)
- QG research is about ‘what is’
  - Not about what ‘could be’
  - Not about ‘what should be’
Heritability of ADHD is 70% \(\rightarrow\) the disorder has genetic origins in 70% of individuals with ADHD. (Wrong!)

- **Heritability**
  ... does not refer to a certain individual, but to individual differences in the population
  ... estimates the **proportion of variance** (=individual differences) in a population attributable to genetic differences
Nature–nurture misunderstandings (3)

Low estimates of shared environmental influences mean that parenting does not matter. (Wrong!)

- There are evidence-based parenting interventions (e.g. parent management for ADHD)

- Genetic research provides new ways of thinking about the parenting environment (many environments are experienced differentially)
Take home message

• ADHD is **70% heritable**. We can explain nearly half of this heritability using DNA (‘SNP heritability’).

• Genetic factors may be involved in **why some individuals with ADHD persist whereas others remit**.

• Heritability does not refer to an individual, but to **individual differences** in the general population.

• Genes are **risk factors**. Even highly heritable disorders can be highly responsive to environmental intervention.
Thank you for your attention!