(Twin studies of) ADHD in adults

Henrik Larsson
Dept. of Medical Epidemiology and Biostatistics
Karolinska Institutet
Developmental Twin Study of Attention Problems

High Heritabilities Throughout Development

Zheng Chang, MSc; Paul Lichtenstein, PhD; Philip J. Asherson, PhD; Henrik Larsson, PhD

The heritability of clinically diagnosed attention deficit hyperactivity disorder across the lifespan

H. Larsson¹*, Z. Chang¹, B. M. D’Onofrio² and P. Lichtenstein¹

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- Philip Asherson
- Andrew Merwood
Do we need a heritability study of clinically diagnosed ADHD?
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1. Is needed to explore how genetic factors influence ADHD across different levels of severity

→ ADHD as a categorical disorder vs an extreme of a continuous trait
Do we need a heritability study of clinically diagnosed ADHD?

1. Is needed to explore how genetic factors influence ADHD across different levels of severity

   → ADHD as a categorical disorder vs an extreme of a continuous trait

2. Is needed to resolve inconsistencies regarding the heritability of ADHD in adults
1. Genetic factors across levels of severity
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Continuous trait measures of ADHD

Burt, 2009
1. Genetic factors across levels of severity

Categorical measures of ADHD

<table>
<thead>
<tr>
<th>Study</th>
<th>Heritability%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burt, 2009</td>
<td>70</td>
</tr>
<tr>
<td>Lichtenstein, 2010</td>
<td>80</td>
</tr>
<tr>
<td>Sherman, 1997</td>
<td>80</td>
</tr>
<tr>
<td>Thapar, 2000</td>
<td>80</td>
</tr>
</tbody>
</table>
Consistent with the hypothesis that ADHD is the extreme of a continuous trait.
However… limitations…

→ Broad categories that contain milder and sub-threshold cases

→ Lacked information on age of onset and impairment criteria
1. Genetic factors across levels of severity

- However… limitations…
  - Broad categories that contain milder and sub-threshold cases
  - Lacked information on age of onset and impairment criteria

- Thus..
  - More stringent diagnostic methods and narrow definitions of ADHD may generate different heritability estimates
2. The heritability of ADHD in adults
2. The heritability of ADHD in adults

The graph shows the heritability percentages for ADHD in adults, with the following data:

- **van den Berg, 2006**: Heritability of 35%
- **Boomsma, 2010**: Heritability of 25%
- **Larsson, 2013**: Heritability of 45%
2. The heritability of ADHD in adults

Substantially lower compared to twin studies among children and adolescents

Heritability %

van den Berg, 2006  Boomsma, 2010  Larsson, 2013
2. The heritability of ADHD in adults

But, it has been difficult to resolve if the drop in heritability reflect developmental changes or relate rater effects
2. The heritability of ADHD in adults

- Dutch and UK twin studies (Kan et al 2013; Merwood et al 2013)
  - Heritability of self-rated ADHD was low in adulthood and in childhood
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  - Heritability of self-rated ADHD was low in adulthood and in childhood

- Swedish longitudinal twin study; Chang et al (2013)
  - Heritability of ADHD in adults was substantial (78%) when both self and parent ratings were combined into a composite index of ADHD
2. The heritability of ADHD in adults

Shared view of parent and self ratings
2. The heritability of ADHD in adults

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- Together this indicate that the low heritability for ADHD in adults is best explained by rater effects
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  → But, a twin study of clinically diagnosed ADHD in adults is needed to close this question
Aim

- Estimate the heritability of clinically diagnosed ADHD across the life span with a specific focus on ADHD in adults
Aim

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  1. Based on similarities in the heritability estimates between continuous trait measures and broad categorical definitions, we expect high estimates also for clinically diagnosed ADHD
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- Estimate the heritability of clinically diagnosed ADHD across the life span with a specific focus on ADHD in adults

1. Based on similarities in the heritability estimates between continuous trait measures and broad categorical definitions, we expect high estimates also for clinically diagnosed ADHD

2. Based on recent cross-informant twin studies, we predict high heritability also for ADHD in adults
   - Cross-informant measures and clinical diagnosis both focus on pervasive symptoms
Sample and measures

- Twins born between 1959 and 2001 from the Swedish Twin Registry with known zygosity

- Clinical data of ADHD diagnosis was available from 1997-2010
  - Diagnosis of ADHD according to ICD-10 (Patient Register; 1997-)
  - ADHD medication (Prescribed Drug Register; 2005-)
## Sample and measures

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>ADHD%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total sample</strong></td>
<td>59,514</td>
<td>1.45%</td>
</tr>
<tr>
<td>(1959-2001)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td>37,714</td>
<td>0.72%</td>
</tr>
<tr>
<td>(1959-1991)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Children and adolescents</strong></td>
<td>21,800</td>
<td>2.71%</td>
</tr>
<tr>
<td>(1992-2001)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Results: Tetrachoric within-twin pair correlations**

<table>
<thead>
<tr>
<th></th>
<th>MZM</th>
<th>DZM</th>
<th>MZF</th>
<th>DZF</th>
<th>Opposite-sex twins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetrachoric</td>
<td>0.90</td>
<td>0.48</td>
<td>0.81</td>
<td>0.50</td>
<td>0.49</td>
</tr>
<tr>
<td>correlations (95% CI)</td>
<td>(0.84-0.94)</td>
<td>(0.33-0.61)</td>
<td>(0.68-0.90)</td>
<td>(0.28-0.67)</td>
<td>(0.40-0.58)</td>
</tr>
</tbody>
</table>
### Results: Model fitting results of univariate analysis of the full sample

<table>
<thead>
<tr>
<th>Model</th>
<th>-2LL</th>
<th>df</th>
<th>$\chi^2$</th>
<th>$\Delta$df</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saturated model</td>
<td>8092.5</td>
<td>59489</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>1. ACE Univariate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full sex-limitation model$^a$</td>
<td>8112.0</td>
<td>59505</td>
<td>19.5</td>
<td>16</td>
<td>-12.5</td>
</tr>
<tr>
<td>Common effects sex-limitation model</td>
<td>8112.0</td>
<td>59506</td>
<td>19.5</td>
<td>17</td>
<td>-14.5</td>
</tr>
<tr>
<td>Null model</td>
<td>8113.5</td>
<td>59509</td>
<td>21.0</td>
<td>20</td>
<td>-19.0</td>
</tr>
<tr>
<td><strong>2. AE Univariate</strong></td>
<td></td>
<td></td>
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<tr>
<td>Null model</td>
<td>8113.7</td>
<td>59510</td>
<td>21.3</td>
<td>21</td>
<td>-20.7</td>
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Results: Best fitting model

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<th>Non-Shared environment (95% CI)</th>
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<tr>
<td>2. ADHD in Adults (1959-1991)</td>
<td>0.74 (0.59-0.85)</td>
<td>0.26 (0.15-0.41)</td>
</tr>
</tbody>
</table>
Conclusions and implications

- Heritability of clinically diagnosed ADHD is high across the life span

  1. Similar heritability estimates for continuous trait measures, broad categorical definitions and narrow diagnostic definitions provide further support for ADHD as the extreme of a continuous trait

  2. High heritability for ADHD in adults indicate that the previous reports of low heritability is best explained by rater effects

- Molecular genetic studies of ADHD in adults
  - Use cross-informant data that are developmentally informative (age-of-onset or longitudinal data)
Did I convince you?