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ADHD symptoms and early institutional deprivation

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B L Developmental Brain-Behaviour Laboratory

Outline

- ADHD Aetiology: Genetic and environmental factors
- English & Romanian Adoptees Study (ERA)
- Is there an association between early deprivation and ADHD?
- Evidence for genetic moderation.
- Summary and future directions.

ADHD: *Aetiology*

- ADHD is an early onset neurodevelopmental disorder involving inattention, hyperactivity and impulsivity
- Strong evidence for large genetic contribution to susceptibility for ADHD – around 75%
- Molecular genetic studies identified multiple genes of small effect –dopamine and serotonin neurotransmitter systems
- Environmental factors also implicated - largely prenatal and perinatal adversity

→ *Shift toward causal mechanism involving interplay between multiple genetic and environmental risk factors to produce a range of liability*

ADHD: *Gene-environment interplay* Recent evidence

- DAT1 interacts with environmental risk factors to influence ADHD symptom scores:

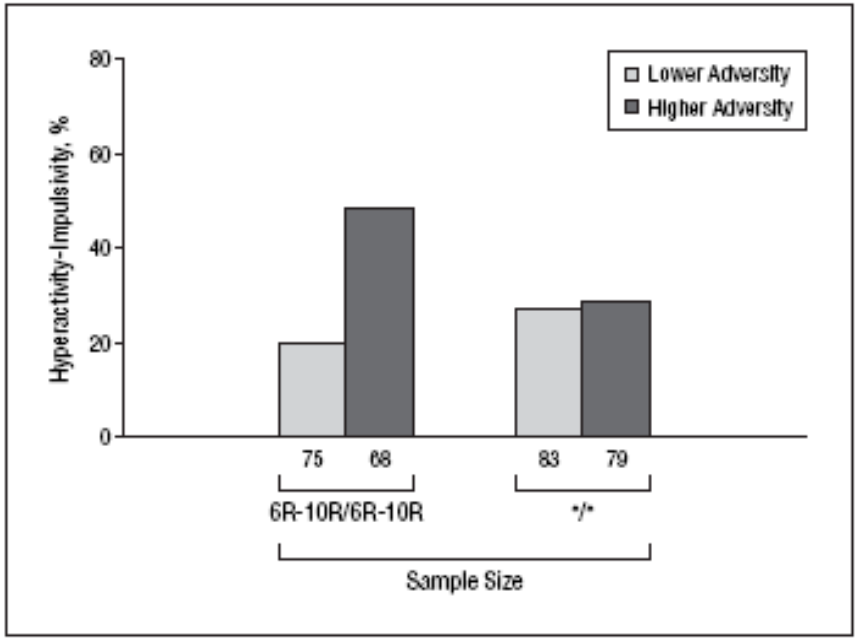
1. maternal prenatal smoking (Kahn et al., 2003)
2. maternal prenatal alcohol use (Brookes et al., 2006)
3. early adversity (Laucht et al., 2007)

A number of polymorphisms seem to be implicated – 10R DAT1 40-bp (3'UTR), 6R DAT1 30-bp (intron 8) & DAT1 10R-6R haplotype

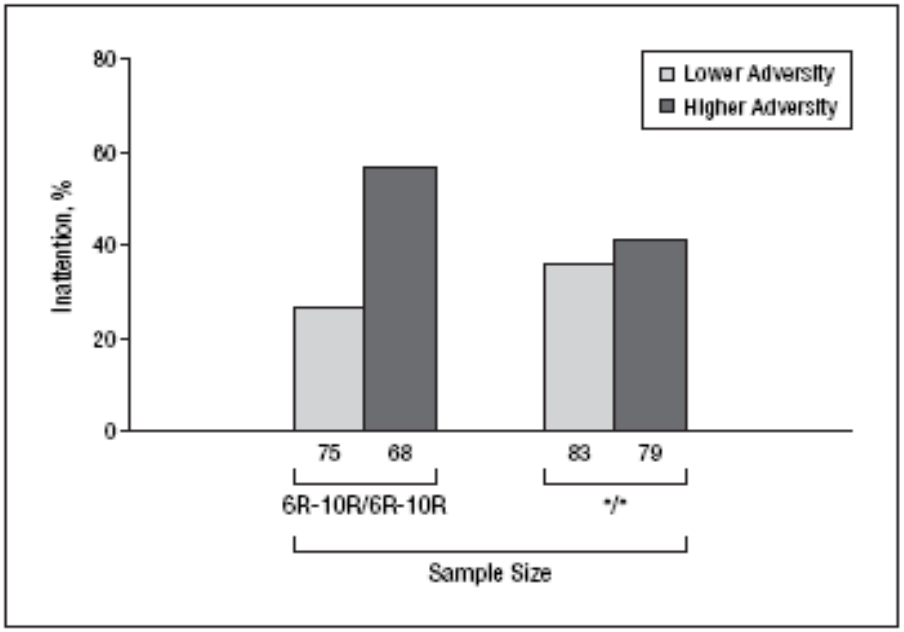
ADHD: *Gene-environment interplay*

- Recent evidence that genes might moderate the impact of early stress and e'risks associated with ADHD

Hyperactivity/impulsivity



Inattention



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Laucht, et al., 2007; Arch Gen Psyc. 64: 585-590

English & Romanian Adoptees Study

- 'Natural experiment': Profound deprivation followed by above average rearing in UK families. = opportunity to study effects of radical environmental change on child development.
- Children placed in institutions in early infancy (so no selection on basis of child impairment)
- Duration of deprivation is largely a function of the child's age at the time of the fall of Ceaucescu regime
- Change of environment rapid and easily timed
- Longitudinal data allows study of within-individual change

ERA Study: *Sample and Design*

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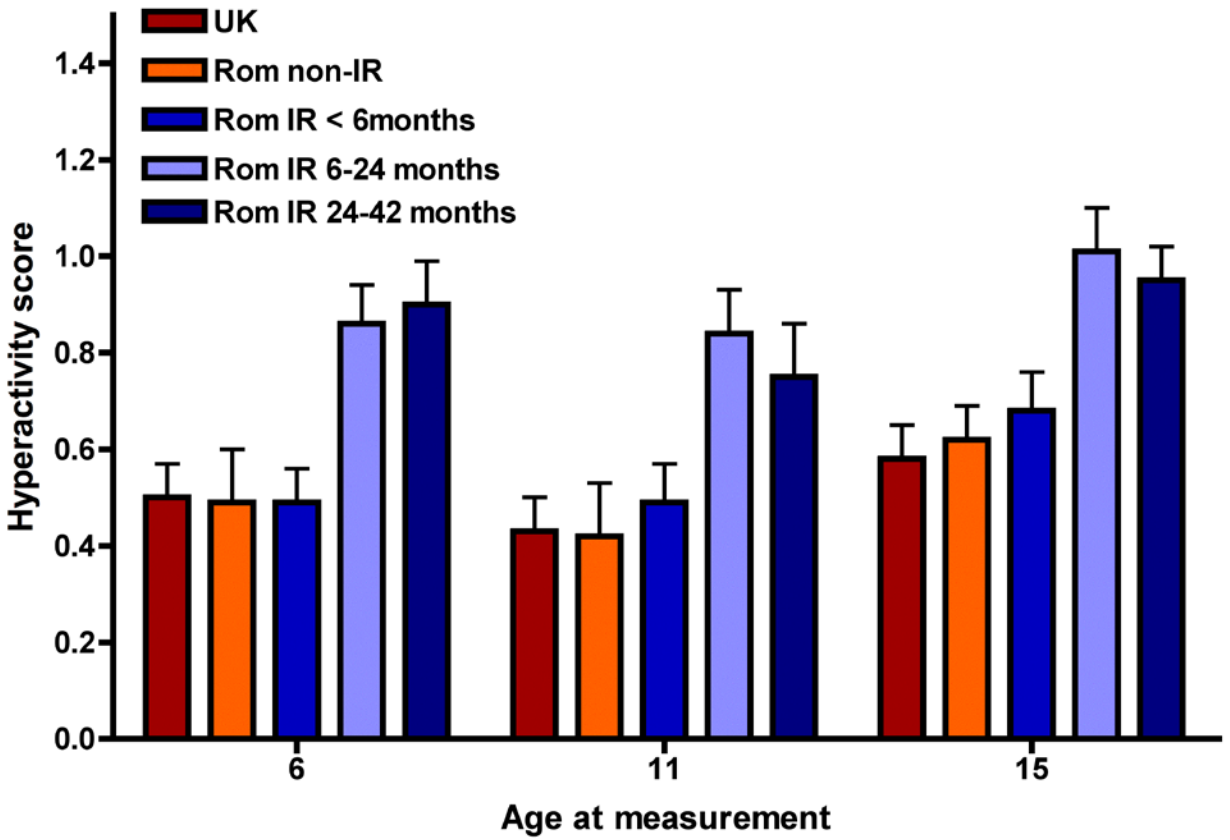
Sample: n = 217	Assessments (years) 4	6	11	15
52 UK adoptees: <6 months	x	x	x	x
58 Romanian adoptees:< 6 months	x	x	x	x
59 Romanian adoptees: 6- <24 months	x	x	x	x
48 Romanian adoptees: >= 24 months		x	x	x

- Includes 21 Romanian children adopted (between 0-42 months) straight from families, who did not experience institutional rearing
- Selected from 324 children processed by the DoH/Home Office between Feb 1990 and Sept 1992 using stratified random sampling strategy
- **98.2%** retention rate by age 11 years

Research Questions

1. Is there an increased risk from institutional deprivation for ADHD?
2. Does deprivation-related ADHD share features with 'normal' ADHD?
3. How does ADHD relate to other deprivation outcomes?
4. Do genetic factor interact with early deprivation to increase the risk for IOI over time?

Is there an increased risk for ADHD following early deprivation?



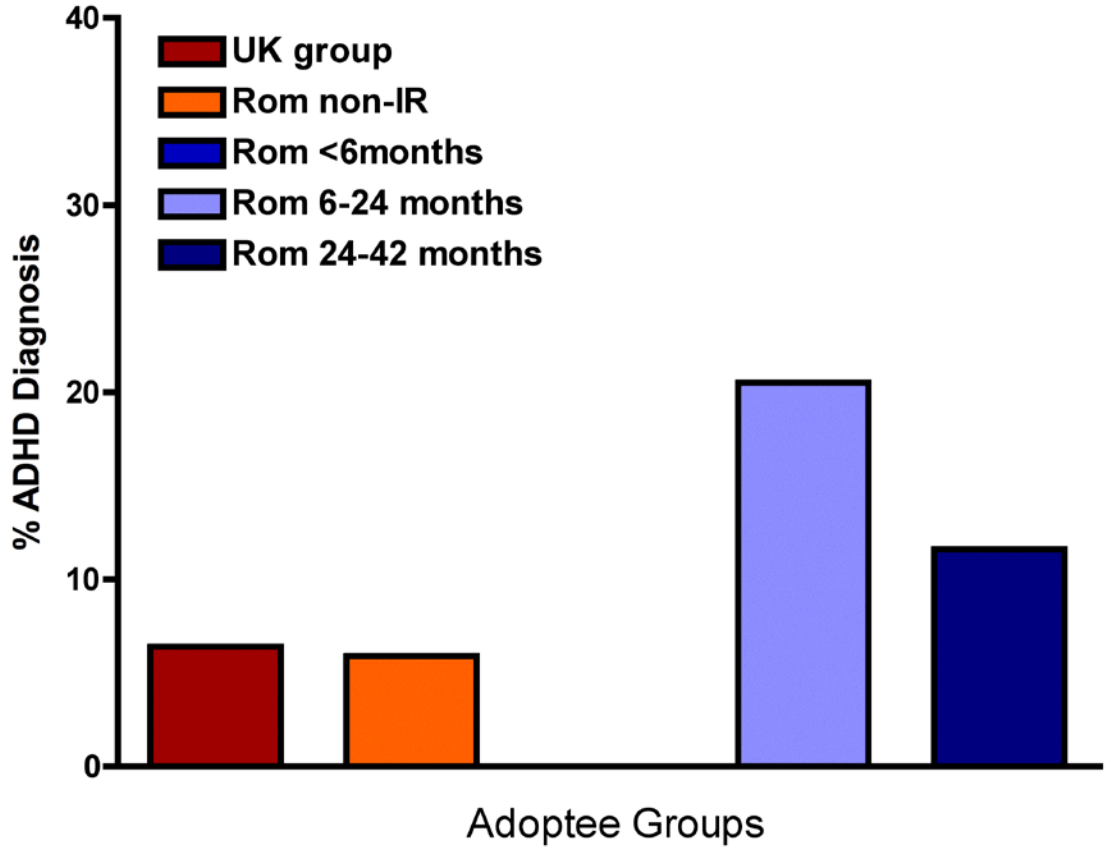
Parent report (shown)
repeated measure analysis:

$F(4,167)=6.77$ $p<.001$

Teacher report (not shown)
repeated measures analysis

$F(4,127)=9.42$, $p<.001$

Is this translated in to more ADHD diagnoses?



CAPA interview age 15 (parent report):

X^2 (4, n=195)=12.07, p=.02

21% with over >6 months had sought help for ADHD

11 percent had received Medication.

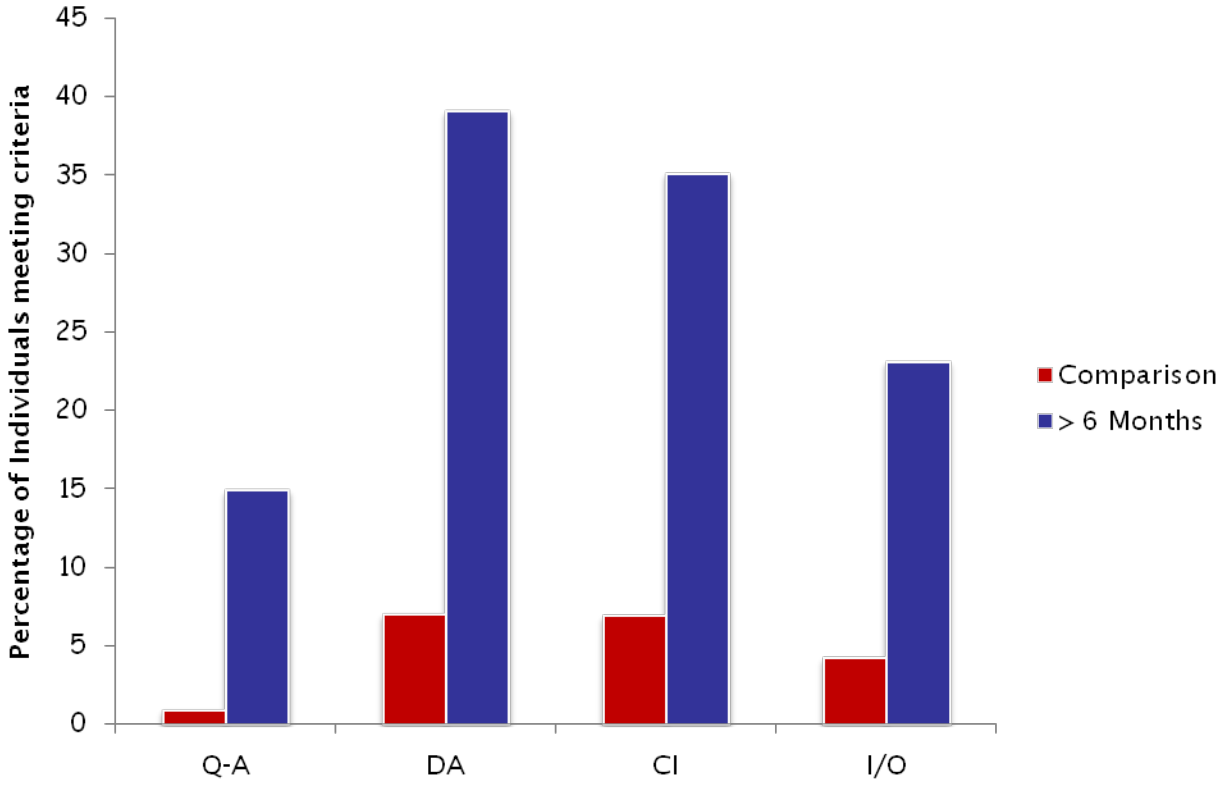
Does derivation-related ADHD share features with 'normal' ADHD?

There appears to be a pattern of distinctive and overlapping elements.

- Is associated with conduct problems which precede it developmentally.
- Although there are no sex differences at 6 these emerge later on.
- There is no relationship with IQ and EF in the study but overall they are more impaired.
- There is a potentially distinctive overlap with disinhibited attachment.

Stevens et al., (2008).

Is Institutional deprivation related to other deprivation-related disorders?



Are the effects moderated by genetic factors?

- ERA provides unique opportunity to study interplay between institutional deprivation and genetic factors in risk for inattention/overactivity
  - well defined social environmental risk
  - longitudinal data
  - variance in outcome

- Rationale for current study of interplay between genetic and environmental risk for ADHD

→ *Does individual genetic variation play a role in susceptibility or resistance to adverse early social environmental risk?*

Dopamine transporter (DAT1) as a good GxE candidate gene

- Evidence from brain imaging/pharmacology:
  - structural and functional abnormalities in dopamine modulated brain circuits.
  - Dopamine transporters main targets for stimulant medication
- Dopamine dysregulation/deficit is a major theory of ADHD aetiology
- Evidence from genetic research
  - Molecular genetic studies showing association with ADHD: some mixed results – evidence of missed GxE?
  - DAT1 = focus for GxE studies of ADHD

D → *extend to extreme social environmental risk factors*

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Summary

- Extended institutional deprivation constitutes a significant risk for ADHD – possible 6 month threshold.

- The effects are
  - Clinically significant
  - long lasting
  - overlapping with other outcomes
  - Distinctive from normal ADHD only to some degree
  - Moderated by genetic factors.

  - Possible mechanism: Early stress related to structural and functional alterations in frontal striatal circuits.

Limitations & future directions

- Limitations:
  - Small sample size
  - Analysis of genetic data possible using ANOVA model
  - Need replication in other institution-reared at-risk samples
- Explore interplay with other candidate genes:
  - Associated with ADHD – e.g. DRD4
  - Genes involved in the stress response system – e.g. glucocorticoid receptor
- GxE in relation to other outcomes

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