Adverse Childhood Experiences and the Origins of Adult Disease
Evidence from the Dunedin Study

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introduction

enduring effects of child stress

timing matters

developing allostatic load

conclusions
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MIND & BODY
CHILD STRESS AND HPA AXIS

AMYGDALA, HIPPOCAMPUS

Hypothalamus
Releasing factor
Anterior pituitary
ACTH (through blood)
Adrenal cortex
Cortisol

> Innate immunity

- Body physical barriers
  (e.g., skin, gastrointestinal tract)

- Non-self recognition
  (complement system, Toll-like receptors)

- Activation
  (cytokines, endothelial cells)

- Response
  (phagocytes, acute phase proteins)
INFLAMMATION & DISEASE

INFLAMMATION REGULATION

STRESS

SYMPATHETIC

GLUCOCORTICOID

PARASYMPATHETIC

+ -
INFLAMMATION REGULATION AND CHILD STRESS
CHILD STRESS AND DISEASE RISK

> Increased adult risk for:

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic lung disease</td>
<td>3.9</td>
<td>[2.6-5.8]</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2.2</td>
<td>[1.3-3.7]</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.9</td>
<td>[1.3-2.7]</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.6</td>
<td>[1.0-2.5]</td>
</tr>
</tbody>
</table>

THE EPIGENETIC LANDSCAPE

Genes

E1 (t1)
E1 (t2)
E2 (t3)

TIME (age)

ADULT DISEASE RISK

Waddington CH, 1975
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Representative birth cohort followed up from birth to age 32y
N=972 (at age 32 years)
Childhood maltreatment (multiple informants, multiple time points)
High-sensitivity CRP (>3mg/dL, cont), fibrinogen, white blood cell count
Risk factors and potential mediating variables throughout life-course
Cox, OLS regression analysis
CHILDHOOD MALTREATMENT
AGE 3-11 YEARS

Maternal rejection (14%)
Harsh discipline (10%)
Disruptive caregivers changes (6%)
Physical abuse (4%)
Sexual abuse (12%)

0 1 ≥2
No Probable Definite
MALTREATMENT AND ADULT INFLAMMATION
HIGH RISK GROUP FOR CARDIOVASCULAR DISEASE (CDC, AHA)

Danese A et al, PNAS 2007, 104:1319-24
MALTREATMENT AND ADULT INFLAMMATION
CO-OCCURRING EARLY-LIFE RISKS

Low birth weight. RR = 1.60 [1.00-2.57]
Low child SES. RR = 1.96 [1.19-3.25]
Low child IQ. RR = 1.44 [1.03-2.01]

Low birth weight. RR = 0.87 [0.49-1.53]
Low child SES. RR = 1.89 [1.50-2.39]
Low child IQ. RR = 2.12 [1.56-2.87]

*Low birth weight. RR = 1.60 [1.00-2.57]
*Low child SES. RR = 1.96 [1.19-3.25]
*Low child IQ. RR = 1.44 [1.03-2.01]
MALTREATMENT AND ADULT INFLAMMATION
ADULT STRESS EXPOSURE

- Low adult SES. RR = 1.48 [1.23-1.73]
- Major Depression. RR = 1.46 [1.10-1.94]
- High Perc. Stress. RR = 1.43 [1.12-1.82]

Low adult SES. RR = 1.44 [0.94-2.20]
- Major Depression. RR = 1.45 [1.06-1.99]
- High Perc. Stress. RR = 1.45 [1.08-1.94]

RR = 1.64 [1.13-2.40]
RR = 1.80 [1.26-2.58]
MALTREATMENT AND ADULT INFLAMMATION
ADULT HEALTH & HEALTH BEHAVIOURS

*CV risk cluster.       RR = 2.38 [1.84-3.10]
*Smoking.                RR = 1.18 [0.69-2.03]
*Physical inactivity.  RR = 1.57 [1.05-2.34]
*Diet.                        RR = 1.01 [0.68-1.48]

RR = 1.76 [1.23-2.51]
RR = 1.80 [1.26-2.58]

*CV risk cluster.       RR = 1.48 [1.10-2.00]
*Smoking.                RR = 1.91 [1.13-3.23]
Physical inactivity. RR = 0.87 [0.69-1.11]
Diet.                        RR = 0.98 [0.78-1.23]

*CV risk cluster.       RR = 2.38 [1.84-3.10]
Smoking.                RR = 1.18 [0.69-2.03]
*Physical inactivity.  RR = 1.57 [1.05-2.34]
Diet.                        RR = 1.01 [0.68-1.48]
MALTREATMENT AND ADULT INFLAMMATION

Danese A et al, PNAS 2007, 104:1319-24
SUMMARY (1)

> Maltreated children show a significant and graded elevation in inflammation levels 20 years later, in adulthood.

> The effect of childhood maltreatment on adult inflammation is independent of the influence of co-occurring risk factors.

> 10% of the cases of inflammation in the population may be attributable to childhood maltreatment.
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Waddington CH, 1975
CHILD STRESS vs ADULT STRESS

Danese A et al, Arch Gen Psychiatry 2008, 65: 409-15
CHILD STRESS vs ADULT STRESS

Danese A et al, Arch Gen Psychiatry 2008, 65: 409-15
> Stress in childhood may modify developmental trajectories and have long-term effect on disease risk.

> If stress does modify developmental trajectories, more favourable conditions later in life may have little effect on disease risk.

> Stress later in life may have a smaller effect on disease risk, because it acts on a more developed system.
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ADULT DISEASE RISK

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TIME (age)

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Waddington CH, 1975
CHILD EXPERIENCES AND ADULT HEALTH
MALTREATMENT, SOCIOECONOMIC DISADVANTAGE, SOCIAL ISOLATION

Danese A et al (submitted)
CHILD EXPERIENCES AND ADULT HEALTH
MALTREATMENT, SOCIOECONOMIC DISADVANTAGE, SOCIAL ISOLATION

> DEVELOPMENTAL:
family history,
birth weight,
child BMI

Danese A et al (submitted)
CHILD EXPERIENCES AND ADULT HEALTH
MALTREATMENT, SOCIOECONOMIC DISADVANTAGE, SOCIAL ISOLATION

> DEVELOPMENTAL:
family history,
birth weight,
child BMI

> CURRENT:
SES,
smoking,
physical activity,
diet

Danese A et al (submitted)
SUMMARY (3)

> Different adverse childhood experiences do not necessarily overlap, and should be tackled independently.

> Adverse childhood experiences influence the development of different stress-sensitive systems.

> The effect of adverse childhood experiences on stress-sensitive system is independent from established (and less preventable) developmental and adult risk factors.
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CONCLUSIONS

> Inflammation could be an important biological mediator of the effect of childhood maltreatment on adult health.

Danese A et al, PNAS 2007, 104:1319-24
> Effective preventive strategies for adult disease should start from an early age.

Danese A et al, *Arch Gen Psychiatry* 2008, 65: 409-15
CONCLUSIONS

> The promotion of healthy psychosocial experiences for children is a necessary, and potentially cost-effective, target for the disease prevention.

Danese A et al (submitted)
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