Biological explanations of links between childhood adversity and later self-harm: a focus on inflammation

Abigail Russell
Senior Research Associate, Centre for Academic Mental Health

@DrAbbyRussell @SASHBristol a.e.russell@bristol.ac.uk
Abigail Russell, Jon Heron, David Gunnell, Tamsin Ford, Gibran Hemani, Carol Joinson, Paul Moran, Caroline Relton, Matthew Suderman and Becky Mars

Centre for Academic Mental Health, Population Health Sciences, University of Bristol Medical School
NIHR Biomedical Research Centre at the University Hospitals Bristol NHS Foundation Trust and the University of Bristol.
University of Exeter College of Medicine and Health
MRC Integrative Epidemiology Unit, University of Bristol Medical School; Population Health Sciences, University of Bristol Medical School

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Childhood adversity

- Adverse childhood experiences “ACEs”
- Household dysfunction and child maltreatment

Number of publications with “adverse childhood experiences” in the title or abstract by year.

Source: https://www.ncbi.nlm.nih.gov/pubmed
The ‘original’ ACEs study

Adversity, self-harm and suicide

Childhood household dysfunction and risk of self-harm: a cohort study of 107,518 young adults in Stockholm County
Emma Björkenstam¹,², Kyrriaki Kosidou³,⁴ and Charlotte Björkenstam⁶

Suicide among youth – etiology, and treatment
Christine B. Cha,¹ Peter J. Franz,² Eleonora M. Guzmán,¹ Catherine R. Glenn,³ Evan M. Kleiman,² and Matthew K. Nock²

Childhood maltreatment
There is strong evidence indicating that various forms of childhood maltreatment such as sexual, physical, and emotional abuse predict future suicidal ideation and suicide attempt among youth. Prospective cohort studies and twin studies have demonstrated the unique
Biological embedding of early adversity

- Epigenetic changes
- Altered HPA axis reactivity
- Altered neural structure and function
- Chronic inflammation
  - The immune system and inflammatory response involve a host of cells, cytokines and other molecules that act to fight infection

Linking inflammation and behaviour

- The brain recognises signals from the immune system
- This can lead to changes in mood and behaviour
- ‘Sickness behaviour’ triggered by pro-inflammatory molecules:
  - Fever
  - Decreased appetite
  - Depression
  - Suicidal behaviour
Childhood adversity and inflammation

- C-reactive protein
- Interleukin-6


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Inflammation and suicidal behaviour

- Meta-analysis of inflammatory markers and suicidal ideation, suicidal behaviour or suicide (n=18)
- Blood levels of IL-6 and CRP were significantly increased in participants with suicidality compared to controls
- Small effect size estimates: IL-6 $g=0.3$, CRP $g=0.45$
- In children and adolescents (n=2)
- One study found no difference in IL-6, one found higher IL-6 IL-1β and TNFα


Do high levels of inflammatory markers mediate the association between ACEs and self-harm?

- The Avon Longitudinal Study of Parents and Children (ALSPAC)
- Born in Bristol and Avon 1991-1992
- Initially ~14,000 children
- Information from 4,308 young people used in the current study

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Childhood adversities ages 0-9: reported by mother, partner, young person

Blood samples age 9 ½

Self-harm reported by young person age 16

Covariates and intermediate confounders

Sensitivity analyses: self-harm with suicidal intent at 16, self-harm at 21, multiple self-harm in past year at 16, excluding those with psychiatric disorder, excluding those with high CRP indicating acute infection, using the mdNLR as an alternate measure of inflammation
### Childhood adversity

<table>
<thead>
<tr>
<th>Adverse childhood experience</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual abuse</td>
<td>0.8</td>
</tr>
<tr>
<td>Physical abuse</td>
<td>7.6</td>
</tr>
<tr>
<td>Emotional abuse</td>
<td>19.1</td>
</tr>
<tr>
<td>Parent substance use</td>
<td>11.7</td>
</tr>
<tr>
<td>Parent mental health problems or suicide attempt</td>
<td>39.3</td>
</tr>
<tr>
<td>Violence between parents</td>
<td>21.7</td>
</tr>
<tr>
<td>Parental separation</td>
<td>21.6</td>
</tr>
<tr>
<td>Child experiences bullying</td>
<td>12.7</td>
</tr>
<tr>
<td>Parent criminal conviction</td>
<td>6.6</td>
</tr>
</tbody>
</table>

![Bar chart showing frequency of adverse childhood experiences](bristol.ac.uk)
<table>
<thead>
<tr>
<th>ACE</th>
<th>Definition</th>
<th>Number of questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual abuse</td>
<td>Was the child sexually abused</td>
<td>7</td>
</tr>
<tr>
<td>Physical abuse</td>
<td>Whether physically cruel to child</td>
<td>31</td>
</tr>
<tr>
<td>Emotional abuse</td>
<td>Whether or not mum/partner had been emotionally cruel to the child</td>
<td>32</td>
</tr>
<tr>
<td>Parent substance use</td>
<td>Daily use of cannabis or any use of other drugs. Or, alcohol problem by self-reported problematic use, and saw a doctor because of it</td>
<td>62</td>
</tr>
<tr>
<td>Parent mental health problems or suicide attempt</td>
<td>Depression scores (EPDS&gt;12) and medication, presence of schizophrenia, bulimia, anorexia or attempted suicide.</td>
<td>57</td>
</tr>
<tr>
<td>Violence between parents</td>
<td>Parent experienced physical cruelty from partner, or displayed (specific types) of violence towards partner</td>
<td>43</td>
</tr>
<tr>
<td>Parental separation</td>
<td>Parents divorced or separated. Degree to which this impacted on the child.</td>
<td>32</td>
</tr>
<tr>
<td>Bullying</td>
<td>Child bullied</td>
<td>6</td>
</tr>
<tr>
<td>Parent convicted</td>
<td>Parent convicted of offence</td>
<td>18</td>
</tr>
</tbody>
</table>
Mediation analysis

ACEs
Age 0-9 years

Inflammatory markers
Age 9 ½ years

Self-harm
Age 16 years
Results

ACEs

Inflammatory markers

Indirect effect
RR 1.00
95% CI 1.00, 1.01

Direct effect
RR 1.11
95% CI 1.05, 1.18

Self-harm
Sensitivity analysis:
suicide attempt

ACEs

Inflammatory markers

Suicide attempt

Direct effect
RR 1.22
95% CI 1.11, 1.33

Indirect effect
RR 1.00
95% CI 1.00, 1.01
Altered inflammatory response rather than systemic inflammation?

Timing of measures

Prior studies detecting inflammatory consequences of self-harm?

Population-based vs clinical samples
In conclusion...

- Young people who have been exposed to childhood adversity are a group at high risk of self-harm.
- The association between ACEs and self-harm does not appear to be mediated by an inflammatory process in childhood.
- Further research is needed to identify alternative psychological and biological mechanisms underlying this relationship.
Thank you

and thanks to the ALSPAC team and participants, the MRF and MRC, and Becky Mars (PI), Jon Heron, David Gunnell, Tamsin Ford, Gibran Hemani, Carol Joinson, Paul Moran, Caroline Relton and Matthew Suderman

a.e.russell@bristol.ac.uk
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