Pathways to Aggressive Behaviour During First Episode Psychosis
A Report from the UK National EDEN Study

Max Birchwood

www.youthspace.me
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- Vimal Sharma
- Nick Freemantle
Christina Edkins inquiry finds missed opportunities to prevent killing

Report makes 51 recommendations after homeless man with mental health issues stabbed schoolgirl in Birmingham last year

- Organisations failed to listen to and respond to carers and significant others consistently and adequately.

- The accessing and sharing of information between key agencies was ineffective.

- Organisations' information-recording and storage were not robust enough to allow good management and care.

- Services need to be more proactive in making it easier for a person with mental health issues to engage with them.

The chair of the investigation panel, Dr Alison Reed, said: "Many different organisations are associated with this very sad and complex case. It is clear that there were missed opportunities."
• Why do individuals act on their delusions and others resist?
• What are the developmental pathways to harm to self or others?
• Why are there no interventions to reduce harm vs treating psychosis? Are they the same thing?
• Can we prevent such behaviour?

Christina, a bright pupil who hoped to become a nurse or carer, got on the number 9 bus in Birmingham city centre on the morning of 7 March last year and sat on the top deck. Simelane, wearing all the clothes he had for
Pathways to Violent Behavior During First-Episode Psychosis: A Report From the UK National EDEN Study

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Supplemental content at JAMAPsychiatry.com

Original Investigation

IMPORTANCE. Although many studies have explored the correlates of violence during first episode psychosis (FEP), most have simply compared violent psychotic individuals with nonviolent psychotic individuals. Accumulating evidence suggests there may be subgroups within psychosis, differing in terms of developmental processes and proximal factors associated with violent behavior.

OBJECTIVE. To determine whether there are subgroups of psychotic individuals characterized by different developmental trajectories to violent behavior.

DESIGN, SETTING, AND PARTICIPANTS. The National EDEN (Evaluating the Development and Impact of Early Intervention Services in the West Midlands) Study longitudinal cohort assessed premorbid delinquency (premorbid adjustment, adaptation and scale across childhood and adolescence), age at illness onset, duration of untreated psychosis, past drug use, positive symptoms, and violent behavior. Group trajectories of premorbid delinquency were estimated using latent class growth analysis, and associations with violent behavior were quantified. This study included 6 early intervention services in 5 geographical locations across England, with violent behavior information available for 670 first psychotic episodes.

MAIN OUTCOMES AND MEASURES. Violent behavior at 6 or 12 months following early intervention services entry.

RESULTS. Four groups of premorbid delinquency were identified: stable low, adolescent-onset high to moderate, stable moderate, and stable high. Logistic regression analysis, with stable low delinquency as the reference group, demonstrated that moderate (odds ratio, 1.53; 95% CI, 1.03-2.25) and high (odds ratio, 3.53; 95% CI, 1.85-6.73) premorbid delinquency trajectories increased the risk for violent behavior during FEP. After controlling for confounders, path analysis demonstrated that the increased risk for violence in the moderate delinquency group was indirect (partially mediated by positive symptoms) (probit coefficient [B] = 0.12; P < .001); while stable high delinquency directly increased the risk for violence (B = 0.38; P < .05).

CONCLUSIONS AND RELEVANCE. There appear to be diverse pathways to violent behavior during FEP. Stable high premorbid delinquency from childhood onwards appears to directly increase the risk for violent behavior, independent of psychotic risk-related factors. In addition to tackling illness-related risks, treatments should also directly address antisocial traits as a potent risk for violence during FEP.

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Meta-analysis

A systematic review and meta-regression analysis of aggression during the First Episode of Psychosis


Objective. The First Episode of Psychosis (FEP) represents a period of heightened risk for aggression. However, it is not known whether this risk is significantly altered following contact with mental health services.

Method. Meta-analytic methods were used to estimate pooled prevalence of ‘any’ and ‘serious’ aggression during FEP, while meta-regression analyses were conducted to explore reasons for heterogeneity between studies.

Results. Fifteen studies comprising 3,294 FEP subjects were analysed. Pooled prevalence of any aggression before service contact was 28% (95% CI: 22-34) and following contact 31% (95% CI: 20-42). Pooled prevalence of serious aggression was 16% (95% CI: 11-20) before service contact and 13% (95% CI: 6-20) following contact. Four studies reporting repeated assessments within the same cohort revealed that aggression rates did not significantly differ post and pre-service contact. Odds Ratios for any aggression: 1.18 (95% CI: 0.46-2.99) and serious aggression: 0.61 (95% CI: 0.31-1.21).

Conclusion. Rates of aggression are high during FEP, both before and following initial service contact, and seem not to alter following contact. This conclusion remains tentative due to considerable heterogeneity between studies and a lack of prospective cohort studies.

Summations

- High rates of aggression are observed during first episode psychosis (FEP).
- Rates of aggression during FEP appear not to substantially alter following service contact.

Considerations

- Extant studies of aggression during FEP are heterogeneous in the assessment and reporting of aggressive acts.
- More prospective studies are needed in which the effects of specific interventions for aggression during FEP are evaluated within same patient cohorts.

Winsper et al. (2013) JAMA Psychiatry, 70 (12) 1287-1293
Background

• Rates of violence/aggression during FEP do not appear to substantially decrease following service contact (Winsper et al. 2013)

• Mirrors concerns that treatments for psychosis do not tackle associated violent behaviour (Serper et al., 2011)
Background

• The aetiology of violent/aggressive behaviour during psychosis is heterogeneous.

– The causes underlying the behaviour may differ
– There are at least two distinct pathways:
  • Violence associated with premorbid conditions (e.g., antisocial traits)
  • Violence associated with acute psychopathology (e.g., positive symptoms)
It has been hypothesized that there are 3 groups of violent psychotic individuals:

1. The early starters display a pattern of antisocial behaviour emerging in childhood, which remains relatively stable across the lifespan.
2. An illness onset group displays no antisocial behavior prior to illness, then repeatedly engages in aggressive behavior.
3. A second illness onset group displays no antisocial behaviour prior to and for the first few decades of illness, then commits serious violence.

In the Dunedin prospective study:

40% of individuals who developed schizophreniform disorder by age 26 years displayed conduct disorder prior to the age of 15.1 (p<0.001)


12. Hodgins S, Cree A,
Research Questions

Are there distinct subgroups of FEP patients differing in premorbid delinquency patterns?

Do these subgroups differ in prevalence of violent behavior following EIS entry?

What are the direct and indirect (via mediators, e.g., positive symptoms) associations between premorbid delinquency and violent behavior?
Data Resource

**National EDEN:** Evaluating the Development and Impact of Early Intervention Services in the UK (more details see: Birchwood et al., 2014, EIP)

Longitudinal cohort of FEP patients across 5 sites in England. 1,027 patients at baseline.

- Baseline
- 6 months
- 12 months
The National/SUPER EDEN sites

Birmingham
5 teams
(Birchwood/Lester)

Lancashire + Wirral
5 teams
(Marshall/Lewis/Sharma)

East Anglia
4 teams
(Jones/Fowler)

Cornwall 2 teams
(Amos)
NIHR SUPEREDEN programme grant
Sustaining Positive Engagement and Recovery
The next step after Early Intervention for Psychosis

Lead: Birmingham and Solihull Mental Health Foundation Trust

Cambridgeshire and Peterborough NHS Foundation Trust EIS
Cheshire and Wirral Partnership NHS Trust EIS
Lancashire NHS Partnership Trust EIS
Norfolk & Waveney Mental Health Partnership Trust EIS
Devon and Cornwall Partnership Trust EIS
University of Birmingham
University of Bristol
University of Cambridge
University of East Anglia
University of Manchester
University of Warwick
King's College London

National Institute for Health Research
Assessments

• **Outcome:** Violent behaviour during EIS contact
  – “Adverse Outcomes Screening Questionnaire”
  – Dichotomous outcome (0=no violence; 1=violence at 6 or 12 months). Shortened version of the MacArthur study questionnaire.

• **Main predictor:** Premorbid delinquency
  – Premorbid Adjustment Scale (PAS) (“adaptation” subscale)
  – Continuous measure at baseline referring to: childhood, early adolescence, and late adolescence
Assessments: Confounders and mediators

• Past Drug Use
  – Continuous measure at baseline (0: no past drug use; 1: not more than 3 times; 2: less than weekly; 3: 1 to 3 times weekly; 4: almost every day)

• Duration of untreated psychosis
  – Dichotomous measure (0: less than 6 months; 1: more than 6 months)
Assessments: Confounders and mediators

• Age of illness onset
  – Continuous measure reported at baseline

• Positive symptoms
  – Positive and Negative Syndrome Scale (PANSS)
  – Continuous measure reported at 6 months
Supplementary Table 1. Attrition analysis comparing those retained in analysis to those lost to follow-up

<table>
<thead>
<tr>
<th>Risk factors for violence</th>
<th>Violent behaviour questions</th>
<th>Associations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Retained $^5$</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td><strong>Premorbid delinquency$^1$</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>low</td>
<td>299 (49.2%)</td>
<td>154 (49.7%)</td>
</tr>
<tr>
<td>adolescent onset</td>
<td>43 (7.1%)</td>
<td>30 (9.5%)</td>
</tr>
<tr>
<td>moderate</td>
<td>187 (30.8%)</td>
<td>84 (26.6%)</td>
</tr>
<tr>
<td>high</td>
<td>79 (13%)</td>
<td>48 (15.2%)</td>
</tr>
<tr>
<td><strong>DUP$^2$</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months</td>
<td>415 (62.7%)</td>
<td>234 (67.2%)</td>
</tr>
<tr>
<td>&gt; 6 months</td>
<td>247 (37.3%)</td>
<td>114 (32.8%)</td>
</tr>
<tr>
<td><strong>Past drug use$^3$</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.00 (1.68)</td>
<td>2.03 (1.68)</td>
</tr>
<tr>
<td><strong>Positive symptoms at 6 months$^4$</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>11.58 (4.34)</td>
<td>11.28 (4.72)</td>
</tr>
<tr>
<td><strong>Age of onset of illness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>21.43 (5.09)</td>
<td>21.15 (4.78)</td>
</tr>
</tbody>
</table>

$^1$ PAS assessed at baseline; $^2$ Duration of untreated psychosis assessed at baseline; $^3$ Past drug use assessed at baseline; $^4$ PANSS scale assessed at 6 months; $^5$ Complete violent behavior information available.
Methods: 3 stages

• Latent Class Growth Analysis: LCGA (Question 1)
  – To group individuals according to patterns of delinquent behavior across time from childhood to late adolescence

• Logistic Regressions (Question 2)
  – To assess unadjusted associations between delinquent groups (identified in the LCGA) and violent behavior during EIS contact

• Path Analysis (Question 3)
  – To assess direct and indirect (via possible mediators, e.g., positive symptoms) associations between delinquent groups and violent behavior
Aggression post FEP

- 13.7% at 6 or 12 months
- 8.6% at 6 months; 8.5% at 12 months
## Supplementary Table 2. Descriptive statistics of violent behavior following EIS contact

<table>
<thead>
<tr>
<th>Type of violent behavior</th>
<th>6 months assessment</th>
<th>12 months assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pushed anyone</td>
<td>39 (5.8%)</td>
<td>47 (6.6%)</td>
</tr>
<tr>
<td>Slapped anyone</td>
<td>11 (1.6%)</td>
<td>13 (1.8%)</td>
</tr>
<tr>
<td>Used knife</td>
<td>2 (0.3%)</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>Choked anyone</td>
<td>4 (0.6%)</td>
<td>6 (0.8%)</td>
</tr>
<tr>
<td>Beaten anyone</td>
<td>43 (6.3%)</td>
<td>49 (6.9%)</td>
</tr>
<tr>
<td>Hit with blunt instrument</td>
<td>7 (1.0%)</td>
<td>7 (1.0%)</td>
</tr>
</tbody>
</table>

### How often harmed others

<table>
<thead>
<tr>
<th>Frequency</th>
<th>6 months assessment</th>
<th>12 months assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once</td>
<td>43 (65.2%)</td>
<td>36 (56.9%)</td>
</tr>
<tr>
<td>2 to 5 times</td>
<td>18 (27.3%)</td>
<td>22 (33.8%)</td>
</tr>
<tr>
<td>Over 5 times</td>
<td>5 (7.6%)</td>
<td>6 (9.2%)</td>
</tr>
</tbody>
</table>

### Who harmed

<table>
<thead>
<tr>
<th>Frequency</th>
<th>6 months assessment</th>
<th>12 months assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family</td>
<td>23 (34.3%)</td>
<td>28 (42.4%)</td>
</tr>
<tr>
<td>Friend</td>
<td>11 (16.4%)</td>
<td>6 (9.1%)</td>
</tr>
<tr>
<td>Healthcare/staff</td>
<td>1 (1.5%)</td>
<td>3 (4.5%)</td>
</tr>
<tr>
<td>Stranger</td>
<td>25 (37.3%)</td>
<td>21 (31.8%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (10.4%)</td>
<td>8 (12.1%)</td>
</tr>
</tbody>
</table>
Results 1: Latent Class Growth Analysis

- Four groups of premorbid delinquency were identified:
  - Stable low (48.5%)
  - Stable moderate (28.7%)
  - Stable high (13.2%)
  - Adolescent onset (9.7%)
Trajectories of Premorbid Delinquency (LCGA)

Assessed using the “adaptation” subscale of the PAS
Results 2: Logistic Regressions

- Stable moderate delinquency significantly increased risk of violent behavior:
  \[
  OR=1.97 \ (95\% \ CI=1.12-3.46) *
  \]

- Stable high delinquency most strongly increased risk of violent behavior:
  \[
  OR=3.53 \ (95\% \ CI=1.85-6.73) *
  \]

* Stable low delinquency used as the reference group. These associations are unadjusted.
Results 3: Direct pathways modelled

Stable high delinquency*

Stable moderate delinquency*

Adolescent onset delinquency*

Past drug use reported at baseline

Positive symptoms at 6 months

Age at illness onset

Violent behavior at 6 or 12 months

Longer DUP at baseline

*Stable low delinquency is the reference group

NB: Direct associations shown for high delinquency only for clarity. Same pathways modelled for other delinquency groups
Results 3: Indirect pathways modelled

Stable high delinquency*

Stable moderate delinquency*

Adolescent onset delinquency*

Past drug use reported at baseline

Positive symptoms at 6 months

Age at illness onset

Longer DUP at baseline

Violent behaviour at 6 or 12 months

*Stable low delinquency is the reference group

NB: Indirect associations shown for high delinquency only for clarity. Same pathways modelled for other delinquency groups
Results 3: Direct Associations

Three factors were independently (i.e., all other factors controlled for) associated with violent behaviour:

Stable high delinquency: $\beta = 0.379$, $p = .05$
Positive symptoms: $\beta = 0.074$, $p < .001$
Early onset of illness: $\beta = -0.044$, $p = .003$
Results 3: Indirect Associations

• Stable moderate delinquency was indirectly associated with violent behavior via positive symptoms: $\beta = 0.119$, $p=.002$

• Stable moderate delinquency increased the risk of violent behavior by increasing the risk of positive symptoms rather than being directly related
Summary

Stable high delinquency independently increased risk of violent behaviour

Stable moderate delinquency only increased risk of violent behavior via positive symptoms (there was no direct association)
Conclusions

Individuals demonstrating antisocial behaviour from childhood onwards may be especially likely to engage in violent behavior during FEP.

Violent behavior in this subgroup appears to be independent of psychosis-related risks (e.g., positive symptoms).

In addition to tackling illness related risks, treatments should directly address antisocial traits.
Opportunity for prevention in those at risk?
Thank you.

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References