Prematurity at birth and adolescent depressive disorder

GEORGE C. PATTON, CAROLYN COFFEY, JOHN B. CARLIN, CRAIG A. OLSSON and RUTH MORLEY

Summary  Association between prematurity/low birthweight and adolescent depressive disorder studied using a case–control design within a prospective cohort study of 2032 adolescents. Odds for depressive disorder were 11-fold (95% CI 2.6–62) higher for the premature/low-birthweight participants after regression adjustment for major confounding factors. For premature/low-birthweight females, cumulative rates of depressive disorder over 30 months were 15.2% (95% CI 11.1–20.5) v. 1.8% (95% CI 1.6–2.1) in those with normal deliveries. Physiological adaptations in utero before full term may be implicated causally in some cases of depression in adolescence.

Declaration of interest  None.

Prematurity and low birthweight have been linked to IQ, attention deficit disorder and emotional problems in children (Bhutta et al, 2002). Two recent studies have suggested an association between birthweight and psychological distress in early adulthood (Cheung, 2002) and middle age (Cheung et al, 2002). The present report addresses the relationship between intra-uterine growth, as measured by prematurity and low birthweight, and depressive disorder in late adolescence, a period of peak incidence for depressive disorder. The current nested study took place between waves 2 and 6. The nested study was open to participants with at least one previous data wave, resulting in 6653 available observations. The mean age (s.d.) at wave 2 was 15.0 (0.4) and at wave 6 it was 17.4 (0.4) years.

The computerised revised Clinical Interview Schedule (CIS–R) identified putative episodes of ICD–10 (World Health Organization, 1992) depressive disorder in the cohort study (Lewis & Pelosi, 1992) for a second-phase face-to-face interview. A sample of CIS–R non-cases was also selected at random from participants in the same school in a 2:1 ratio to cases.

Blinded face-to-face interview included:

(a) Depression and hypomania modules of the Composite International Diagnostic Interview (CIDI, Core Version 1.1; Robins et al, 1988) were used to generate lifetime ICD–10 diagnoses for affective disorder. The CIDI cases were excluded from reselection at later study waves. Two diagnostic categories for depressive disorder were defined: all cases diagnosed by the CIDI and a second category of ‘stable’ depressive disorder that concurrently fulfilled criteria on both the CIS–R and the CIDI.

(b) Recent life events measured using an adapted List of Threatening Experiences Questionnaire (Brugha et al, 1983).

(c) The Parental Bonding Instrument (PBI; Parker et al, 1979) was administered immediately prior to the CIDI.

The cumulative rate of stable depressive disorder (CIS–R and CIDI) over 30 months was 2.1% (95% CI 1.8–2.5) in females and 0.33% (95% CI 0.19–0.54) in males. Cumulative rates of stable depressive disorder in those born at term and those of birthweight ≥2500 g were low: 0.25% (95% CI 0.13–0.5) in males and 1.8% (95% CI 1.6–2.1) in females. Rates were 1.0% (95% CI 0.8–1.3) in premature low-birthweight males and substantially higher at 15.2% (95% CI 11.1–20.5) in premature low-birthweight females.

Matched pairs or triplets for CIDI-defined depressive disorder (i.e. at least one case and one control from a specific school and wave of selection) were available with complete (parental response) data for 63 cases and 112 controls. For stable depressive disorder, 49 cases were matched with 102 controls. On bivariate analysis, prematurity and low birthweight were associated with approximately sixfold (OR=5.7; 95% CI 1.4–2.3) and approximately threefold (OR=2.9; 95% CI 0.6–1.4) increases in the odds of CIDI-defined depressive disorder, respectively.

The potential mediating roles of adverse parenting, heightened responses to social adversity and high levels of pre-existing symptoms were considered in further conditional logistic regression.
models (Table 1). The baseline odds ratio after adjustment for parental education, parental separation, maternal age at birth, maternal smoking in pregnancy, serious illness in the first year of life and parental depressive disorder suggested that either prematurity or low birthweight increased the odds for depressive disorder by >11-fold. Both low maternal care and high control were independently associated with depressive disorder but adjustment did not markedly reduce the association with prematurity/low birthweight. Adjustment for negative life events reduced the association with depressive disorder but the clearest reduction in association occurred with the addition of pre-existing depressive and anxiety symptoms to the model. Models using stable depression as the outcome produced similar findings.

**DISCUSSION**

Prematurity and low birthweight were associated with a substantially higher rate of depressive disorder in adolescence. After adjustment for potential confounders, the odds for depressive disorder were elevated by >11-fold in adolescents born premature or of low birthweight. For females, rates of stable disorder in those born premature or with low birthweight prevalence estimates were 15%, compared with <2% in those with normal deliveries.

Poor maternal bonding through childhood did not appear to be a mechanism for the association between prematurity and depressive disorder. However, adjustment of regression models for pre-existing depressive and anxiety symptoms and recent negative life events did reduce the association, suggesting that a heightened sensitivity to social adversity might play a role in depressive disorder in this group.

Foetal genotype, maternal physiology and placental function may affect early brain development through nutritional and hormonal mechanisms (Leon, 2001). For those born prematurely, perinatal stress and suboptimal nutrition in the early weeks 

### Putative mediators

<table>
<thead>
<tr>
<th>Parenting style</th>
<th>Maternal low care</th>
<th>23 (21)</th>
<th>30 (49)</th>
<th>2.4 (0.7–11)</th>
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<tr>
<td>Maternal high control</td>
<td>25 (23)</td>
<td>32 (52)</td>
<td>2.9 (0.7–7.2)</td>
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<tr>
<td>Negative life events</td>
<td>Single</td>
<td>27 (24)</td>
<td>30 (49)</td>
<td>3.8 (0.6–25)</td>
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<tr>
<td></td>
<td>Multiple</td>
<td>25 (23)</td>
<td>32 (52)</td>
<td>4.4 (0.9–19)</td>
</tr>
<tr>
<td></td>
<td>Previous depression/ anxiety</td>
<td>19 (17)</td>
<td>48 (77)</td>
<td>5.9 (1.3–36)</td>
</tr>
</tbody>
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<tr>
<th>(a) Adjusted for background factors</th>
<th>(b) Complete model</th>
</tr>
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<tr>
<td>OR (95% CI)</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Low birthweight</td>
<td>8 (7)</td>
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</tbody>
</table>

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**REFERENCES**


