# **ORIGINAL ARTICLE**

# Population based, controlled study of behavioural problems and psychiatric disorders in low birthweight children at 11 years of age

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**Objective:** To evaluate the risk of long term behavioural problems and psychiatric disorders associated with being born with low birth weight.

**Design/study groups:** A population based, controlled follow up study at 11 years of age of 130 low birthweight (LBW) children weighing less than 2000 g at birth who were without major handicaps, and a random sample of 131 normal birthweight (NBW) children born at term weighing over 3000 g. **Main outcome measures:** Validated questionnaires addressing behaviour completed by mothers and teachers and child evaluation by child psychiatrist using a semistructured interview.

**Results:** Behavioural problems, as defined by abnormal scores on more than four of 32 measures, were found in 40% of LBW children compared with 7% of NBW children (odds ratio (OR) 8.2, 95% confidence interval (CI) 3 to 25, p = 0001). A psychiatric disorder was diagnosed in 27% of the LBW children compared with 9% of the NBW children (OR 3.1, 95% CI 1.5 to 6.5, p = 0.001). The LBW children were more often inattentive, had social problems, and low self esteem. None of the pre-, neo-, or peri-natal variables in the LBW group were statistically significant predictors of behavioural outcomes or the presence of psychiatric disorders. Behavioural problems and psychiatric disorders were as common in those with birth weight less than 1500 g as those with birth weight 1500–2000 g. **Conclusion:** An increased risk of behavioural problems and psychiatric disorders persists in LBW adolescents.

Behavioural problems and psychiatric disorders are more common in low birthweight (LBW, birth weight < 2500 g) and very low birthweight (VLBW, birth weight < 1500 g) children than those of normal birth weight. Studies, mainly at preschool and early school age, have reported that behavioural profiles associated with VLBW range from externalising behavioural problems (hyperactivity, inattention) to internalising behavioural problems (low self esteem, impaired social skills, withdrawal, depression, and anxiety). 1-15 Psychiatric disorders such as attention deficit hyperactivity disorder (ADHD) and anxiety disorders have been reported in early adolescence. 7 8

The aims of this study were: (a) to test the hypothesis that non-disabled 11 year old children with birth weight less than 2000 g more commonly have behavioural problems and psychiatric disorders than their normal birthweight peers, and to describe the behavioural profile; (b) to evaluate the degree to which behavioural differences, if present, are confounded by parental factors and to control for such factors; (c) to investigate, in explorative analyses, whether identifiable preperi-, or neo-natal factors are predictive of behavioural problems in LBW children; (d) to evaluate whether such behavioural differences are independent of the child's intelligence quotient (IQ).

# **METHODS**

The study and control groups have been more fully described in a previous study (table 1). All surviving children weighing less than 2000 g born in the County of Hordaland, Norway, between 1 April 1986 and 8 August 1988, and without major handicaps such as cerebral palsy, blindness, deafness, multiple malformations, or chromosomal aberrations, were the basis of this study. Of the 217 liveborn LBW children, 21 were excluded because of major handicaps (12 cerebral palsy, eight chromosomal aberration, and one blind). The control children were

partly based on a random sampling from a defined geographical region (non first born), and partly as every 40th child born at the regional hospital. In addition, birth weight had to be above 3000 g, length of gestation more than 37 weeks, and there had to be no requirement for transfer to the neonatal unit.<sup>17</sup> The regional ethics committee on medical research approved the project protocol, and written consent was obtained from all children and parents.

Cerebral ultrasound was performed on all infants with birth weight less than 1500 g (n = 50) at two days, one week, and two to three weeks, and cerebral haemorrhage was classified as described by Papile *et al* (Table 1).<sup>18</sup>

Behavioural and personality characteristics of the children were assessed with the children behaviour check list, administered to mothers, and the teacher's report form, administered to teachers. <sup>19 20</sup> To focus specifically on attention deficit disorder (ADD) and ADHD, the psychometric scales of the Yale children's inventory were administered to mothers. <sup>21–25</sup> Social skills, in terms of Asperger or autism related problems, were investigated using the psychometric scale of the Asperger syndrome diagnostic interview (ASDI), consisting of 27 items (see data supplement on www.archdischild.com). <sup>26</sup>

The first author performed a semistructured interview of all children according to the children assessment schedule (CAS). This interview generates scores for 11 areas of the child's life: school, friends, activities, family, worries, anxieties, self esteem, behavioural mood, somatic complaints, aggressive behaviour, and thought problems.<sup>27</sup> The individual

**Abbreviations:** LBW, low birthweight; VLBW, very low birthweight; ADHD, attention deficit hyperactivity disorder; IQ, intelligence quotient; ADD, attention deficit disorder; ASDI, Asperger syndrome diagnostic interview; CAS, children assessment schedule

Table 1 Pregnancy, perinatal and neonatal data for 130 intact low birthweight infants assessed at 11 years of age (children without cerebral palsy, blindness, deafness, mutiple malformations, or chromosomal abberations)

	All (n= 130)	<1500 g (n=50)	1500-1999 g (n=80)
Prenatal factors			
Twin or triplet pregnancy	26 (20)	7	19
Pre-eclampsia Pre-eclampsia	41 (32)	21	20
Placental abruption	10 (8)	2	8
Maternal smoking in pregnancy	45 (41)	18	27
Intrauterine stress*	19 (16)	11	8
Chorioamnionitis†	15 (12)	7	8
Breech presentation	26 (23)	13	13
Intrapartum stress leading to delivery‡	13 (11)	5	8
Prenatal continous variables, mean (SD)			
Birthweight ratio§	0.83 (0.19)	0.83 (0.19)	0.83 (0.19)
Birth head-circumference ratio§	0.98 (0.06)	0.98 (0.06)	0.98 (0.06)
Birth length ratio§	0.95 (0.07)	0.96 (0.08)	0.95 (0.07)
Birth and neonatal factors			
Vaginal delivery	39 (33)	12	27
Apgar score at 5 minutes <7	13 (10)	10	3
Seizures/abnormal neurological signs	1 (1)	1	0
Pulmonal air leaks	3 (2)	3	0
Bronchpulmonary dysplasia¶	13 (11)	12	1
BPD steroid treated	2 (2)	2	0
Neonatal systemic bacterial infection**	8 (6)	6	2
<30% breastmilk in neonatal ward	35 (27)	12	23
Boy/girl	66/64	26/24	40/40
Birth/neonatal continous variables, mean (SD)			
Maximum bilirubin concentration	192 (60)	176 (52)	203 (62)
Days to regain birth weight	10 (5)	11 (5)	10 (5)
Apgar at 5 minutes	8 (1)	8 (1)	9 (1)
Days of assisted ventilation or oxygen††	6 (13)	13 (18)	1 (4)
Cerebral ultrasound performed in all with birth weight <1500 g (n=50):‡‡			
Grades I-II haemorrhage	12		
Grades III–IV haemorrhage	1		
Permanent dilation of ventricles§§	2		

Unless otherwise indicated, values are numbers or numbers with percentages in parentheses.

\*Pathological non-stress test or low hormones.

 $\uparrow$ High C reactive protein, temperature >38,5° C, smelly fluids or combinations of these and premature rupture of the membranes.

‡Abnormal cardiotocogram leading to caesarean section or forceps delivery.

§Birth weight divided by the 50th centile birth weight for that gestational age (similar for head circumference and birth length).

¶Two of these needed oxygen supplementation after 40 weeks postmenstrual age.

\*\*Proven by positive blood or spinal fluid culture or suspected because of symptoms and blood infection parameters.

††Number of days on ventilator + number of days on continuous positive airways pressure + number of days on supplemtary oxygen.

scores represent the summed number of items where problems are identified (see data supplement on www.archdischild.com). After the interview, the child psychiatrist scored items based on the child's behaviour during the prior interview. Information from both of these two parts of the CAS forms the basis for psychiatric diagnoses in the diagnostic and statistical manual of mental disorders (see table 33).28 29 The child psychiatrist was blinded to birthweight status in all cases.

On all behavioural scales and items, a higher score indicated more problematic behaviour. For all scales a score higher than the 90th centile for the control children of the same sex was classified as abnormal (see data supplement on www.archdischild.com). The number of abnormal scores for each child was added up to obtain an overall measure of abnormal child behaviour (total problem score). A total problem score higher than the 90th centile for the control children of the same sex was classified as abnormal.

Psychometric intelligence was assessed using four subscales from the WISC-R.30 The LBW children had a mean prorated IQ that was significantly lower than that of the controls: 96 and 101 IQ points respectively (95% confidence interval (CI) for the difference 2.1 to 7.7, p = 0.001). 16

Data on parental and family characteristics and child rearing methods were obtained at the time of the 11 year examination using the child rearing practices report, the parental stress inventory, and the symptom check list-revised

(SCL-90-R).31-35 Maternal problem solving abilities were assessed by the Raven progressive matrices administered at the time of the five year follow up examination (see table 2).36

# Statistical analysis

The main statistical analyses were performed as in the study at 5 years of age and in seven stages.15 First, the numbers of LBW and control children with abnormal behavioural scores were compared using  $\chi^2$  tests. Second, the odds ratios (ORs) from these analyses were adjusted for confounding by parental factors using multiple logistic regression analyses (SPSS 10).37 Third, interactional effects between parental factors and birth weight were investigated, with total problem score as outcome variable. Fourth, to investigate whether LBW children were more at risk than control children when more than one parental risk factor was present, a cumulative parental risk score was computed. Interaction between this variable and birth weight was examined. Fifth, the proportions of LBW boys and girls with abnormal behavioural scores were compared. Sixth, the proportion of children with abnormal total problem scores was compared for LBW children with birth weight less than or above 1500 g. Seventh, the relation between the identified pregnancy, birth and neonatal variables and abnormal total problem score among LBW children was investigated using multiple logistic regression analysis.

<sup>‡‡</sup>None had periventricular leucomalacia.

<sup>§§</sup>Both had intraventricular haemorrhage.

BPD, Bronchopulmonary dysplasia.

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Table 2 Parental and family characteristics and child rearing practices in the low birthweight and control families

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	<2000 g (n=130) Mean (SD)	>3000 g (n= 130) Mean (SD)	Difference of means	95% CI of difference	p Value (t test)		
Parental							
Paternal education in years	12.1	13.3	1.3	0.5 to 2.1	0.002		
Average income (in 1000 no.kroner)	40.9 (2.8)	45.5 (4.1)	4.6	-1.4 to 5.3	0.36		
Maternal education in years	12.3	13.3	1.0	0.4 to 1.7	0.002		
Maternal age (years)	31.7 (5.2)	32.6 (4.5)	0.9	-0.4 to 2.2	0.15		
Maternal psychological distress*¶	0.34 (0.33)	0.27 (0.24)	0.07	-0.14 to 0.007	0.07		
Maternal Raven score†	-0.08 (1.0)	0.14 (1.0)	0.21	-0.48 to 0.05	0.11		
Child rearing practices‡¶							
Nurturance	-0.13 (0.09)	0.14 (0.08)	-0.27	-0.51 to -0.03	0.03		
Restrictiveness	0.08 (0.10)	-0.07 (0.08)	0.15	-0.09 to 0.40	0.27		
Permissiveness	0.03 (0.09)	-0.03 (0.08)	0.06	-0.19 to 0.31	0.63		
Overruling	0.08 (0.09)	-0.09 (0.08)	0.16	-0.08 to 0.41	0.19		
Parent domain stress§¶	0.08 (0.1)	-0.07 (0.09)	0.15	-0.12 to 0.42	0.28		
Family life event§¶	1.3 (1.4) Number (%)	1.2 (1.4)	0.03 p Value (χ²)	-0.33 to 0.39	0.87		
Single parent family	15 (12)	10 (8)	0.3				
Maternal smoking during pregnancy	55/111	38/125	0.04				

<sup>\*</sup>Symptom check list-revised (SCL-90R). General stress index.

## **RESULTS**

All eligible children from the study at 5 years of age (174 eligible of 217 live born) were still eligible at 11 years of age according to the stated criteria. A total of 130 of 174 (75%) eligible LBW children and 130 of 170 (76%) eligible control children were examined at a mean age of 11.3 years (SD 1.5 months). Of the 44 LBW children not examined, 20 did not want to participate, 12 did not answer, seven had moved, and five could not be traced. Of the 40 controls not examined, 17 did not want to participate, 11 did not answer, four had moved, and eight could not be traced.

In the families of the LBW children, mean paternal and maternal education was lower, parental stress somewhat higher, child rearing more often seemed less nurturing, and maternal smoking in pregnancy was more common. Consequently, the possible confounding effects of these factors were investigated. The LBW and the control families were comparable for the other background variables (table 2).

For the 130 LBW children who completed all the behavioural questionnaires, mean (SD) birth weight was 1537 (367) g and mean (SD) gestational age 32 (3) weeks. Eighty had birth weights between 1500 and 1999 g, 36 between 1000 and 1499 g, and 14 below 1000 g. Sixty six of the LBW children (51%) and 69 of the controls (53%) were boys. Apart from one child with neonatal seizures, none had any abnormal neurological signs in the neonatal period. Ten of the 50 VLBW children had grade I cerebral haemorrhage, two had grade II, none had grade III, and one had grade IV. None had periventricular leucomalacia. Of the 13 with haemorrhage, two had permanent dilatation of the ventricles.

More LBW than control children had abnormal scores for attention, social problems, and anxiety/depression scales of the child behaviour check list. More LBW children had abnormal scores for most of the Yale children's inventory scales. Only one LBW child (1%) and none of the controls met the criteria for Asperger syndrome according to the ASDI questionnaire. Teachers reported that more LBW children had abnormal scores for social problems, attention problems, and delinquent behaviour on the teacher's report form. According to the CAS, the LBW children themselves more often reported problems in the areas of school (including academic performance and inattentive behaviour), spare time activities, aggressive behaviour, and lower self esteem compared

with the control children (data supplement on www.archdischild.com). More than four abnormal scores for boys and girls represented the 90th centile cut off level for having an abnormal total problem score. Forty per cent of the LBW children and 7% of the controls had abnormal total problem scores, with little change after adjusting for confounding parental factors or child IQ (data supplement on www.archdischild.com).

Thirty three (27%) LBW children met the clinical criteria for a child psychiatric disorder compared with 12 (9%) controls (OR 3.1, 95% CI 1.5 to 6.5, p = 0.001) according to the CAS. For 13 of the 33, the psychiatric disorder was ADHD (table 3). No comorbid disorder (more than one psychiatric disorder) was diagnosed within the ADHD group. Of the 101 LBW children with available total problem score and CAS psychiatric evaluation, 40 had an abnormal total problem score, with approximately half of these having a psychiatric disorder (table 4). Every fourth LBW child had an attention problem according to the children behaviour check list, but only every fourth of these was in turn classified with hyperactivity disorder by the child psychiatrist. Four (4%) of the LBW children were referred to a child psychiatric outpatient clinic (all were diagnosed as having ADHD according to the clinic) compared with three (2%) of the control children (OR 1.5, 95% CI 0.3 to 6.7, p = 0.62).

Those children behaviour check list scales with significant differences between LBW and control children were investigated further to assess overlap of behavioural problems. The highest correlation was found between the attention scale and the social problem scale (r = 0.7, p = 0.0001).

There were no significant differences in the proportion of LBW boys compared with LBW girls with abnormal outcome measures except that 15% of LBW boys and 5% of girls had an ADHD diagnosis (OR 2.2, 95% CI 0.8 to 6.1, p=0.054) according to the CAS.

No significant interactions were found between birth weight and parental factors. In univariate analyses, a higher level of maternal psychological distress and parental stress, lower family income, single parent family status, and higher scores on the child rearing practices report factor scales restrictiveness and permissiveness were significantly associated with having abnormal total problem scores in the combined LBW and control group. These parental factors were therefore used to calculate the cumulative parental risk score.

<sup>†</sup>Raven progressive matrices test. The age corrected scores, z-transformed to mean of 0 and SD of 1, were used.

<sup>‡</sup>Child rearing practices report (CRPR).

<sup>§</sup>Parental stress index. Parental domain score reflects aspects of general parenting

<sup>¶</sup>Factor scores z-transformed to mean of 0 and SD of 1 were used.

Table 3 Child psychiatric diagnoses according to DSM-III-R from the CAS interview

Diagnosis	No <2000 g (%)	No >3000 g (%)	OR (95% CI) Unadjusted	p Value (χ²)	OR (95% CI) Adjusted for parental factors*	p Value (logistic regression)
Depression	2 (2)	1 (1)	2.0 (0.2 to 23)	0.5	1.8 (0.2 to 21)	0.52
Separation anxiety	3 (2)	2 (2)	1.5 (0.3 to 9.4)	0.6	0.4 (0.01 to 19)	0.66
Phobia	9 (7)	7 (5)	1.3 (0.5 to 3.7)	0.6	0.9 (0.2 to 3.3)	0.87
Enuresis	2 (2)	1 (1)	2.1 (0.2 to 23)	0.5	1.8 (0.2 to 21)	0.52
Encoprese	2 (2)	0				
Attention deficit hyperactivity disorder	13 (10)	1 (1)	14.7 (1.8 to 114)	0.001	9.6 (1.2 to 82)	0.04
Oppositional defiant disorder	1 (1)	0				
Conduct disorder	1 (1)	0				
Total number of diagnoses	33 (27)	12 (9)	3.1 (1.5 to 6.5)	0.001	2.4 (1.01 to 5.5)	0.047

<sup>\*</sup>Adjusted for paternal education, maternal education, child rearing practices (nurturance), smoking in pregnancy, sex, life events, and maternal psychological distress.

DŚM-III-R, Diagnostic and statistical manual of mental disorders, 3rd revision; CAS, children assessment schedule.

**Table 4** Child psychiatric diagnoses for the low birthweight children with behavioural problems\*

Children with abnormal total problem score	No	Yes	Total
Children with psychiatric disorder			
No	55	23	<i>78</i>
Yes	6†	1 <i>7</i>	23
Total	61	40	101

<sup>\*</sup>Only those with available total problem score and psychiatric evaluation were included.

There was no significant interaction between the risk score and birth weight.

Among the LBW children, neither having a VLBW (< 1500 g) nor abnormal neonatal cerebral ultrasound was associated with increased frequency of abnormal total problem scores. Mean prorated IQ was similar in LBW children with normal and abnormal total problem scores.

In the multiple logistic regression analysis, none of the prenatal or neonatal variables were predictors of behavioural problems or psychiatric disorders at age 11.

# **DISCUSSION**

In this study, 40% of the LBW children compared with 7% of the control children were classified as having behavioural problems. Mothers indicated that the LBW children more often had attention, social, and anxiety problems, whereas teachers indicated delinquency, social, and attention problems. The findings were similar for LBW girls and boys. Behavioural problems were not associated with lower IQ. The child psychiatrist found that three times as many LBW children had a psychiatric disorder, with ADHD as the main disorder. Adjusting for confounding parental factors did not influence these findings substantially.

A behavioural profile with attention and social problems was most common among the LBW children with behavioural problems in this study. In a study of VLBW children and controls at 12 years of age, Botting *et al*<sup>6</sup> found that 28% had a psychiatric disorder, which is comparable to the findings of our study. In that study, every fourth VLBW child was classified as having an ADD, but no differentiation was made between those with and without hyperactivity. In our study a very similar proportion of children were inattentive, but few (one in ten) were hyperactive. This supports previous research suggesting that attention problems without hyperactivity (ADD) are more typical than "classical" ADHD in LBW children.<sup>2 6 9</sup>

Like Botting *et al*<sup>6</sup> and Szatmari *et al*,<sup>2</sup> we found no increased risk of comorbid conduct disorders for the LBW children with

ADHD and ADD. Lack of social skills and difficulties in relating to peers have been described in previous studies.<sup>12</sup> <sup>14</sup> <sup>15</sup> <sup>38</sup> <sup>39</sup> These findings were affirmed by our study. However, we found only one LBW child with Asperger syndrome according to the ASDI questionnaire, indicating that the lack of social skills is not similar to Asperger/autism. A high correlation between social problems and attention problems in terms of distractibility, impulsivity, and lack of adaptability in our study may indicate that inattention may be the primary issue for the LBW child. Possibly having difficulties with adaptability, impulsivity, and sustaining attention is the cause of difficulties in relating to peers and the cause of lower self esteem and lower social activity level in the present study.<sup>40</sup>

Only 4% of the LBW children had previously been referred to a psychiatric specialist. As 40% of the LBW children had abnormal total problem scores, this may indicate that many have behavioural problems that are difficult to detect or are different from or less severe than those thought to benefit from psychiatric referral. It should be emphasised that the abnormal total problem score is a statistical construct and not validated in terms of severity of the behavioural problems. The abnormal total problem score OR of 8 compared with the individual subscales with OR of 2–5 may indicate that, even though attention deficits and social problems are the most common problems, no specific pattern of behavioural problems is present. The large variety of behavioural problems in LBW children is a challenge to parents, teachers, and social workers who have to provide help for the individual child.

In this study, we found three times as many LBW as control children suffering from a psychiatric disorder, which is similar to previous findings. However, we did not find more severe psychiatric disorders, such as psychotic disorders and manic-depressive disorders. Such disorders are uncommon at this age. Precursors of such disorders may be thought problems, anxiety, and withdrawal, which in this study were 2–4-fold higher in LBW than control children. Further studies when the children are older are needed to disclose such problems.

Our findings do not support an interaction between birth weight and parental risk factors, which is in accordance with previous studies.<sup>3,7,11</sup> We did not evaluate the significance of genetic factors as they are notoriously difficult to investigate. Genetic factors are another strong factor of individual variation in child development. In the last decade, the role of genetic influences in child psychopathology has been emphasised; in particular, ADHD and autism have been shown to have strong heritable components.<sup>42–45</sup>

A calculation based on the numbers from this study indicates that there would be about 43 new LBW children with behavioural problems every year in our county, but 420 new normal birth weight children with comparable problems. We maintain that the focus should be on identifying and alleviating behavioural problems in all children, regardless of birthweight group.

Two had enuresis, two encoprese, and two phobia.

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