Birth weight and cognitive function in young adult life: historical cohort study

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Abstract

Objective: To examine the relation between birth weight and cognitive function in young adult life.
Design: Retrospective cohort study based on birth registry data and cognitive function measured during evaluation for military service.
Subjects: 4300 Danish conscripts born between 1973 and 1975.
Main outcome measures: Mean score in the Boerge Prien test of cognitive function; score is the number of correct answers to 78 questions and correlates with full scale intelligence quotient (IQ).
Results: Mean score in the Boerge Prien test increased from 39.9 at a birth weight of ⩽2500 g to 44.6 at a birth weight of 4200 g even after adjustment for gestational age and length at birth, maternal age and parity, and other variables. Above a birth weight of 4200 g the test score decreased slightly.
Conclusion: Birth weight is associated with cognitive performance in young adult life. Interference with fetal growth may influence adult cognitive performance.

Introduction

Birth weight is associated with the development of coronary heart disease, stroke, and diabetes in adult life,[1] and malnutrition in early life may affect the developing brain.[2 3] However, few data exist on the link between birth weight and later cognitive function. One study found reduced mental development in early childhood in children with a low birth weight, especially if the placenta was normal.[4] In contrast, a recent study reported little association between low birth weight and poor cognitive performance in adult life after adjustment for confounding factors.[5] This study included 1576 men and women born between 1920 and 1943 in Britain, but only 47% of the number invited to participate took the cognitive function test.[5]

With such limited data further population based studies are needed; we therefore examined the relation between birth weight and cognitive performance in young men.

Subjects and methods

We conducted the study in the fifth conscription district of Denmark, which covers mainly the counties of North Jutland and Viborg. The population is about 700 000. Nearly all Danish men have to register with the draft board when they are about 18 and undergo physical and mental examination. We studied all men who were born in Denmark after 1 January 1973 who were drafted from and resided in the study area from 1 August 1993 to 31 July 1994.

All those drafted took a 45 minute validated group intelligence test, the Boerge Prien test, which was developed in 1957 for the Danish draft board.[6] The test includes time limited subtests covering four categories of items: letter matrices, verbal analogies, number series, and geometric figures. The score is the total number of correct answers for 78 questions and is highly correlated with verbal intelligence quotient (IQ) (0.78), performance IQ (0.71), and full scale IQ (0.82) on the Wechsler adult intelligence scale.[6] In the validation study the mean full scale IQ was 105.8 and the mean Boerge Prien test score 44.2.[6]

We linked the data on cognitive function to data from the Danish birth registry by means of personal identification numbers. Since 1968 all Danes have been given a 10 digit personal registration number at birth that is used in all Danish data sources, thus making linkage between registries simple and valid. The birth registry contains information on all births in Denmark since 1 January 1973. Data are obtained from the official reports filed by the midwives attending the delivery; in Denmark all deliveries are attended by a midwife. Birth

Table 1 Mean (SD) score in Boerge Prien test according to birth weight and other variables studied

Variable	No of subjects*	Mean (SD) score
Birth weight (g):		
⩽ 2500	171	39.9 (9.3)
2501-3000	603	42.2 (9.3)
3001-3500	1451	42.6 (9.7)
3501-4000	1453	43.5 (9.4)
4001-4500	515	44.6 (9.6)
>4500	105	44.6 (9.5)
Gestational age (weeks):		
⩾37	3898	43.1 (9.5)
33-36	269	42.2 (9.4)
<33	130	41.6 (10.6)
Length at birth (cm):		
<48	127	40.1 (10.0)
48-49	302	42.4 (8.9)
50-51	1057	42.0 (9.8)
51-53	1491	43.2 (9.5)
54-55	998	44.3 (9.5)
>55	345	43.8 (9.3)
Mother		
Marital status:		
Married	3520	43.3 (9.6)
Unmarried, divorced	780	42.1 (9.8)
Age (years):		
<25	1740	42.3 (9.6)
25-29	1636	43.7 (9.7)
>29	921	43.3 (9.2)
Parity:		
0-1	3006	43.0 (9.6)
2	817	43.2 (9.7)
⩾3	475	43.1 (9.1)
Employment:		
Unemployed, housewife, retired	1121	41.7 (10.3)
Employed	2954	43.6 (9.3)
Self employed, assisting spouse	223	42.8 (9.0)

*Total number of subjects for each variable is not always 4300 because of missing data.

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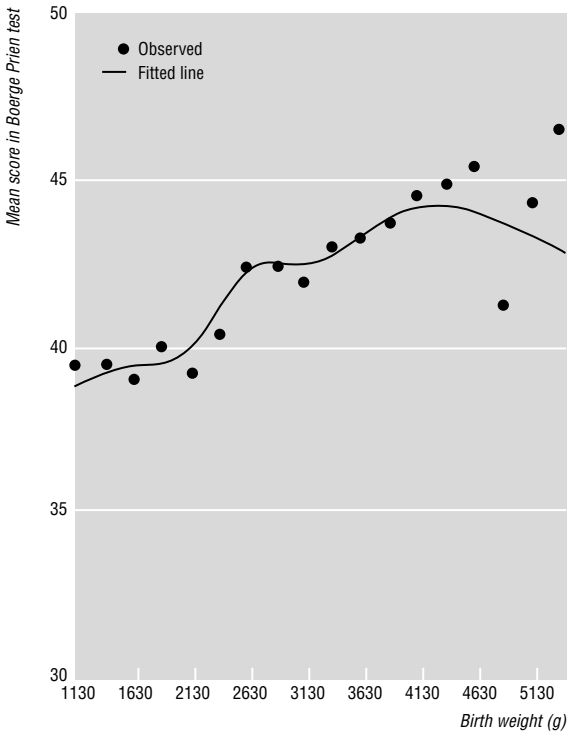

Fig 1 Estimated and observed mean score in Boerge Prien test of cognitive functioning according to birth weight. Smoothed curve was fitted by unrestricted quadratic spline regression with adjustment for gestational age and length at birth and for maternal age, parity, marital status, and employment

weight is reported in categories of 250 g, and we used the midpoints of the categories in the analyses.

We first analysed the data by estimating the mean score in the Boerge Prien test according to birth weight and for each category of the variables listed in table 1. Since the relation was not linear we then used quadratic spline regression[7] to illustrate the relation. In both analyses we adjusted for length at birth and gestational age and for maternal age, parity, marital status, education, and employment using the values in table 1 as categorised variables.

Results

A total of 5183 men were drafted during the study period. Of these, 4661 underwent a medical examination when drafted, 4300 of them having been born after the start of the computerised birth registry on 1 January 1973. A total of 522 subjects were excused from the examination because of asthma, osteochondrosis, or epilepsy, 505 of them having been born after 1 January 1973.

Mean birth weight in the 4300 subjects born after 1 January 1973 was 3471 (SD 0.54) g and mean length 52.2 (2.4) cm. The mean score in the Boerge Prien test was 43.1 (9.6). Table 1 shows mean scores according to the main study variables. The mean score increased with increasing birth weight and gestational age and with mother's age and occupational status. Figure 1 shows the relation between mean score and birth weight in the measured categories and by quadratic spline regression. Even after adjustment for multiple covariates the mean score in the Boerge Prien test increased with birth weight from 1900 g to 4200 g.

Discussion

In contrast to the findings of Martyn et al,[5] we found positive associations between birth weight within the normal range and cognitive function 20 years later. The association between low birth weight and cognitive function corroborates previous findings.[4] The reduced score in the Boerge Prien test for some men with high birth weights may plausibly be due to the increased risk of underlying diseases or birth traumas.

Olsen and Martyn et al controlled for social class,[4 5] and Olsen also controlled for smoking, alcohol intake, and parents' school education.[4] We also controlled for social factors but not for smoking or alcohol intake. Our population is large and without self selected non-responders. The study includes almost all young men in a well defined region. In the study by Martyn et al 47% of subjects did not respond.[5] The risk of selective survival is probably higher in the English study because the subjects were born when the chances of survival of infants with low birth weight were much smaller than in our cohort. We had information on about 90% of the cohort. Selection bias seems, therefore, unlikely as explanation for the association.

Confounding is certainly a possible explanation for the findings. Our findings, as well as those of Martyn et al,[5] may be confounded by parents' IQ, which we could not examine. Furthermore, we have no data on postnatal factors, such as nutrition[8 9] and stimulation,[10] that may influence cognitive function. Social class is much more homogeneous in Denmark than in Britain, but residual confounding is still possible despite adjustment for the employment and marital status of the mother.

An association between birth weight and cognitive function could be mediated through prenatal and postnatal factors. Lack of nutrition could cause disproportionate fetal growth, causing impaired brain development. A shortage of specific nutrients important for fetal growth and brain development could be a possible mechanism, and n-3 fatty acids may be the best candidate for such an effect. Variables that are important for cognitive functioning postnatally are breast feeding and early psychological stimuli, both of which could be related to birth weight.[8-10]

Key messages

- Low birth weight and proportionate smallness at birth have been associated with poorer cognitive function in early childhood
- Only a few studies have examined whether this association persists into adult life
- This study found that the mean cognitive test score in 4300 Danish conscripts increased up to a birth weight of 4200 g after adjustment for confounders; there was a slight decrease above a birth weight of 4200 g
- Fetal growth seems to influence adult cognitive performance
- If fetal growth has an impact on mental development it has important consequences from the perspective of maternal care

From the perspective of maternal care, it is important to know whether fetal growth has an impact on mental development. Our results support an association between birth weight and cognitive function in adult life, but data from other populations with careful control for confounding factors are needed.

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Association between raised body temperature and acute mountain sickness: cross sectional study

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Fever has long been associated with acute mountain sickness, and the physiologist Angelo Mosso reported that Dr Jacottet, who died in 1891 of presumed high altitude pulmonary oedema on Mont Blanc, had a body temperature of 38.3°C shortly before he died.[1] We studied the association between body temperature and acute mountain sickness, and body temperature and high altitude pulmonary oedema.

Subjects, methods, and results

We studied 60 climbers (mean age 39 (range 20-64) years) at 490 m (Zurich, Switzerland), after rapid ascent within 22 hours to a mountain hut at 4559 m above sea level, and during the subsequent stay there for 72 hours. We examined the climbers at low altitude, two to six hours after arrival at the hut (4 pm to 8 pm; day 1), and each morning (6 am to 9 am) during the next three days (days 2-4). The ethics committee of the University Hospital, Zurich, approved the study.

We assessed symptoms and signs of acute mountain sickness in a clinical interview and scored them as described previously.[2] We classified climbers as healthy or as having mild acute mountain sickness (score ≤ 3) or as having severe acute mountain sickness (4-13). Climbers with at least three of the following symptoms and signs were considered to have high altitude cerebral oedema: headache resistant to paracetamol, vomiting, dizziness, and ataxia. We measured axillary body temperatures in an ambient temperature 18-24˚C. Blood gas pressures were sampled from the radial artery daily, and posteroanterior chest radiography was done at low altitude and on days 2-4. The chest radiographs were analysed as previously described.[3]

To compare the body temperatures in climbers with and without severe acute mountain sickness, we used the value that was associated with the climber's highest score at high altitude. In climbers with cerebral oedema or pulmonary oedema, or both, we recorded the temperature measured when these conditions were diagnosed.

Because of pulmonary oedema or cerebral oedema, or both, 3/60 climbers had to be evacuated by helicopter on day 2, seven on day 3, and five on day 4. Pulmonary oedema was diagnosed by chest radiography in 22 climbers.

Climbers' body temperatures and scores for acute mountain sickness are plotted in figure 1. The mean (SD) increase in body temperature between low and high altitude was 0.5°C (0.6) in climbers with a score ≤ 3, 1.2°C (0.6) in those with a score >3, and 1.7°C (0.5) in those with cerebral oedema (one factor analysis of variance, $P<0.001$). The mean body temperature was 37.9°C in climbers with cerebral oedema, compared with 36.9°C in climbers with a score ≤ 3 (mean difference 1.0°C (95% confidence interval 0.5 to 1.5)), and 37.7°C in climbers with a score >3 and pulmonary oedema, compared with 37.2°C in those without pulmonary oedema (0.4°C (0.2 to 0.7); Mann-Whitney U test, $P=0.005$). The correlation coefficients between the body temperature and arterial oxygen pressure as well as between the body temperature and the radiographic assessment were -0.52 ($P<0.001$) and 0.42 ($P<0.001$) respectively (simple regression analysis).

Comment

We show a strong relation between body temperature, hypoxaemia, and the severity of acute mountain sickness in 60 climbers studied at low and high altitude. The correlations between the body temperature, the score for acute mountain sickness, and the arterial oxygen pressure suggest that a rise in temperature after rapid ascent to high altitude is a sign of acute mountain sickness and is associated with the severity of hypoxaemia.

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