Increased susceptibility to stress at a psychological assessment of stress tolerance is associated with impaired fetal growth

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**Background**
This study aims to investigate the relationship between birthweight and psychological function, as evaluated by the results of a psychological conscript interview and assessment in young males, including an evaluation of stress susceptibility.

**Methods**
We performed a retrospective cohort study based on linked birth registry data and data from an assessment of psychological function during evaluation for military service. In all, 90,651 young males born 1973–1975, for whom birth record data were obtained from the Swedish Medical Birth Register, were investigated in addition to psychological stress susceptibility during their conscript evaluation in 1991–1994. The assessment of psychological functioning score, including the assessment of stress susceptibility, was used as the dependent variable in a multiple regression analysis in combination with the following independent variables: birthweight, adult weight, head circumference at birth, month of birth, gestational age, maternal parity, and maternal age.

**Results**
The mean value was 5.1 (SD 1.9) on the psychological assessment scale (range 1–9) of psychological level of functioning including evaluation of stress susceptibility, and 5.3 (1.6) on the general psychological performance (leadership) profile. A positive association was seen between birthweight and better assessment results up to a level of about 4000 g birthweight, but above that an inverse association was seen. Positive correlations ($P < 0.001$) were seen between psychological assessment score results and birthweight ($r = 0.07$), gestational age ($0.03$), head circumference ($0.05$), and maternal age ($0.11$), but inverse correlations with maternal parity ($–0.11$) and birth month of the offspring ($–0.04$). In multiple regression analyses, the strongest independent correlations were seen between increasing assessment scores and maternal age and birthweight (positive), as well as with maternal parity and offspring adult weight (negative).

**Conclusion**
Young males at conscript testing show a better general psychological functioning score derived from psychological assessment, including evaluation of stress susceptibility, with increasing birthweight up to 4200 g. Above that birthweight an inverse association is noticed. Impaired fetal growth is predictive of suboptimal psychological functioning and increased stress susceptibility in males during early adult life.

**Keywords**
Adolescence, birthweight, conscript, gestational age, male, psychological, stress

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quasi-experimental studies such as the Dutch Hunger Winter 1944–1945 Study, in which no serious effect could be shown for the impact of maternal/fetal malnutrition alone on general cognitive capacities in offspring at follow-up. Thus it is likely that not only adverse factors in early life are of importance but also protective biological or social factors during childhood, e.g. following an initial period of reduced growth.

Children with low birthweight are at an increased risk for poor mental and cognitive performance during childhood, as shown by poor school performance. Not much is, however, known about the long-term consequences for cognitive function into adult life. Previous studies have found either no association (in adults), or a positive association (in young males), between birthweight and cognitive function. Both boys and girls born small for gestational age (SGA) run an increased risk for lower cognitive performance at age 17 and schooling achievements during childhood than those born appropriate for gestational age (AGA). In the UK SGA-children were recently reported to be less likely to hold professional or managerial jobs, and to have lower levels of weekly income at age 26 years, as compared to AGA subjects.

One aspect of cognitive function is coping with stressful situations and threats. Psychosocial stress implies a wide range of possible reactions in different individuals, due to both the total burden of stress perceived (degree, duration, personal meaning), as well as individual cognition and susceptibility to stress. No study, to our knowledge, has so far investigated the relation between birthweight adjusted for gestational age (fetal growth) and the results of a standardized psychological assessment of stress susceptibility.

In Sweden, the existence of national registers of good quality and validity, as well as an individual personal 10-digit code number for each citizen, enables researchers to do register studies on the associations between birthweight and biological and psychosocial variables in adult life. Two registers of importance in this respect are the Swedish Medical Birth Register and the National Register of Military Conscripts, which holds data collected after a psychological assessment and physical evaluation for military service. Earlier studies in Sweden have used the second register for follow-up studies on psychiatric morbidity and drug abuse in males.

The aim of this study was to investigate associations between birthweight adjusted for gestational age, as an indicator of fetal growth, and psychological assessment of stress susceptibility at the time of conscript testing, in a large cohort of young Swedish males in their late teens.

Subjects and Methods

Subjects

We primarily selected 149,378 Swedish males, born in 1973 (n = 51,228), 1974 (n = 51,875), or 1975 (n = 46,275), and registered in the Medical Birth Register (MBR) of Sweden. Birth variables were then compared with variables for the corresponding individuals from the National Register of Military Conscripts (INSARK), obtained in 1990–1994. In Sweden, military service is based upon a draft system and every healthy young man has to undergo an evaluation test at the age of 18 years, or in some cases at a later occasion. Excluded from this test are individuals with a known diagnosis of severe physical or mental handicap.

In all 5718 (3.7%) subjects were recorded in the MBR, but not in the INSARK, because of a pre-test exclusion for some medical reasons, e.g. mental retardation (n = 1,125), asthma bronchiare (n = 676), diabetes mellitus (n = 536), deafness (n = 456), psychiatric disorders (n = 378), cerebral paresis (n = 140), epilepsy (n = 131), cardiac disorder (n = 110), or severe drug abuse (n = 17). Therefore, males registered in both the MBR and the INSARK comprised 143,660 individuals. This cohort has previously been investigated for associations between birthweight and conscript blood pressure.

Birth variables

At birth the following variables were recorded: birthweight (g), head circumference (cm) and gestational age (weeks). Data on maternal age (years) and parity (n) were also available, but no data on parental socioeconomic status or maternal smoking habits. Increased maternal parity could be a possible marker of larger families, which is a finding more prevalent in lower social classes. All available birth data were used and no outliers excluded.

The psychological assessments

The psychological evaluation results were obtained from a standardized psychological interview and assessment issued by the Swedish National Service Administration, including an evaluation of stress susceptibility. During this assessment every conscript meets a psychologist for a semi-structured conversation of 20–25 minutes duration on average. The psychologist first makes a decision of mental fitness for all the boys. Almost 10% of them are considered to have some reduction in this respect, 7% to such a degree that they should be exempted from military service.

All boys are then assessed with regard to their psychological functioning (PF) as a prognosis of their ability to cope with war-time stress. This is documented as a numerical assessment, the 9-grade Stanine scale, with higher values indicating better functioning.

Another such numerical assessment is given regarding leadership ability for about 60% of the boys and defines the possibility of their gaining different leadership positions (group, squad, or platoon). In basic military training terms it means differences between selection for 5 up to 20 months of service. On the basis of these assessment results a general psychological performance (GPP) for leadership evaluation is carried out in those men considered for potential leading military positions, all of whom also firstly had their PF assessed. A similar 9-grade Stanine scale is used, with higher values indicating better GPP. Finally, a formal report on all assessed aspects of mental and cognitive function is written by the psychologist.

The psychological assessment methods (PF, GPP) have previously been described, but details on questions and methodology exist only in Swedish, and mostly constitute classified military information not available to the public. Therefore, test-retest or validation data of the psychological assessments are not available. No traditional technical stress tests (e.g. mental arithmetic test, colour-word test, cold-pressure test) were used. To ensure uniform evaluation of psychological assessment across the six regional conscript test centres in Sweden, a central authority supervises the instruction and training of participating psychologists, supported by a written manual (Lothgius J, chief military psychologist, personal communication).
From our cohort 142,031 young men were evaluated for PF of whom 87,594 (61.7%) also underwent a GPP evaluation, forming the basis for these analyses.

Statistics
The two registers were linked and correlations calculated for different variables using SAS Institute software and SPSS. Bivariate Pearson’s correlations between untransformed variables were calculated. In multiple regression analysis, birthweight was used in two ways, firstly as an independent variable, and secondly as a dummy variable when squared for improving the fit of the non-linear model. Birthweight was also subdivided into decentiles (−2880, 2881–3130, 3131–3300, 3301–3430, 3431–3560, 3561–3680, 3681–3820, 3821–3980, 3981–4200, 4201+ g) in order to show the non-linear relationship to PF and GPP across decentiles in the figures. A P-value less than 0.05 was considered to be significant.

Results
A complete set of combined birth data and psychological functioning (PF) results, including an assessment of stress susceptibility, was obtained from 90,651 individuals.

Mean birthweight was 3543 g (SD 552) after a mean pregnancy time of 39.7 gestational weeks (SD 2.0). Mean value of the PF score was 5.1 (SD 1.9) and of the GPP leadership assessment 5.3 (SD 1.6) (Table 1).

A positive association was seen between birthweight and both PF and GPP scores up to about 4200 g, and after that a levelling off followed by an inverse association (Figures 1 and 2).

Positive correlations (P < 0.001) were seen between PF scores and birthweight (r = 0.07), head circumference (r = 0.05), gestational age (r = 0.03), and maternal age (r = 0.11), but inverse correlations were found with maternal parity (r = −0.11), month of birth (−0.04) and with offspring adult weight (r = –0.02).

In multiple regression analysis, the strongest independent correlations (P < 0.001) were seen between PF score and maternal age and birthweight (positive), as well as with maternal parity and adult weight (negative) (Table 2).

Discussion
This study has shown a positive association between increasing birthweight and results obtained from PF assessment, including an evaluation of stress susceptibility, at a military conscript test in young Swedish males. This is in accordance with what has previously been described in a similar, but much smaller Danish study on the association between birthweight and cognitive function, as measured by a specific written intelligence test. Above a birthweight of 4200 g the mean scores, obtained with different methods and covering different psychological aspects, levelled off and then slightly decreased in a very similar way in both the Scandinavian studies.

The positive correlation between head circumference and test results in this study, independent of gestational age and birthweight, also adds to the assumption that neuroanatomical

Table 1 Biological variables in male subjects, at birth and at the time of military service evaluation—the army conscript test, together with data on maternal age and parity

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variables at birth</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (g)</td>
<td>149,316</td>
<td>3543 (552)</td>
</tr>
<tr>
<td>Gestational time (weeks)</td>
<td>148,310</td>
<td>39.7 (2.0)</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>147,619</td>
<td>34.8 (1.7)</td>
</tr>
<tr>
<td>Maternal age (years)</td>
<td>149,373</td>
<td>26.1 (4.8)</td>
</tr>
<tr>
<td>Maternal parity (n)</td>
<td>98,150</td>
<td>1.81 (0.95)</td>
</tr>
<tr>
<td><strong>Military service evaluation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>140,844</td>
<td>71.4 (11.0)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>140,844</td>
<td>179.6 (6.5)</td>
</tr>
<tr>
<td>BMIa (kg/m²)</td>
<td>140,844</td>
<td>22.1 (3.0)</td>
</tr>
<tr>
<td>PFb scores (range 1–9)</td>
<td>142,031</td>
<td>5.05 (1.91)</td>
</tr>
<tr>
<td>GPPc scores (range 1–9)</td>
<td>87,594</td>
<td>5.30 (1.62)</td>
</tr>
</tbody>
</table>

*Body mass index.

b Psychological functioning (including assessment of stress susceptibility).

c General psychological performance (leadership) evaluation.
development is of importance for both cognitive function and stress susceptibility. Low birthweight has previously been shown to predict inferior intellectual achievement in late adolescent males, independent of parental education, social class, maternal age, and birth order.20

Stress tests have been developed for many purposes, but are often used for physiological measurements in the laboratory setting, e.g. of hormonal activities or cardiovascular responses. The results obtained may sometimes predict later health hazards. Haemodynamic changes during a psychological stress test have, for example, been shown to predict the progression of carotid artery disease, an indicator of cardiovascular disease,21 but not independently the development of blood pressure.22 In our previous study of the same cohort, impaired fetal growth was associated with higher systolic blood pressure at conscript evaluation.16

One possible mechanism for a true association between low birthweight and increased stress susceptibility would be that subjects with a low birthweight or impaired fetal growth are more prone to be neuro-reactive during stress exposure because both the adrenocortical function23,24 and the sympathetic nervous system25 are altered by size at birth. This may later influence the secretion of stress hormones. Raised fasting plasma cortisol levels in adult life are for example related to low birthweight and increased stress susceptibility in males during early adult life.26 It should, however, also be pointed out that the statistical correlations we obtained were weak, which is often the case in large-scale epidemiological studies of this size due to imprecision of measures, random variability, etc. A drawback is the lack of information on social background factors in the study sample. However, another Swedish study has shown that confounding by social factors is not an issue in explaining e.g. the association between birthweight and adult blood pressure.30 This does, however, not rule out the possibility that social factors are important in the association between birthweight and stress susceptibility. On the contrary, social factors can influence cognitive function in several ways, e.g. through nutrition, parental support, social stimulation, schooling, and other learning opportunities. We regret that we presently do not have access to the social data needed to elucidate these associations. One indicator of the role of social factors is, however, the inverse correlation between psychological functioning (stress tolerance) and maternal parity. This may indicate that young men from large families tend to be more susceptible to stress as a reflection of the fact that large families are more prevalent in lower social classes. Another alternative explanation could hypothetically be that first-born sons benefit from an advantage in psychological functioning over younger brothers for a number of potential reasons.

Other aspects of unmeasured confounding could possibly bias our findings. This has to be investigated further in future studies, and similar research undertaken in female populations.

In conclusion, young males at conscript testing show better general psychological functioning as measured by psychological assessment, including evaluation of stress susceptibility, with increasing birthweight up to 4200 g. Above that birthweight an inverse association is noticed. Impaired fetal growth is predictive of suboptimal psychological functioning and increased stress susceptibility in males during early adult life. We hypothesize that birthweight predicts stress susceptibility in adult life, thus linking early growth factors with the psychophysiological response to cognitive handling of perceived stress.

Acknowledgements

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Table 2  Multiple regression analysis with psychological functioning (PF) score as the dependent variable in 90,631 subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta (×10⁻⁵)</th>
<th>SE (×10⁻⁵)</th>
<th>T-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal parity</td>
<td>-450</td>
<td>7.48</td>
<td>-60.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Maternal age</td>
<td>0.0</td>
<td>1.47</td>
<td>58.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>Adult weight</td>
<td>-0.0</td>
<td>0.57</td>
<td>-9.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Birthweight</td>
<td>0.7</td>
<td>0.09</td>
<td>7.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Gestational age</td>
<td>18.3</td>
<td>3.6</td>
<td>-5.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>Head circumference</td>
<td>18.1</td>
<td>3.7</td>
<td>4.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>(Birthweight)²</td>
<td>-0.0</td>
<td>0.0</td>
<td>-4.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Birth month</td>
<td>-0.0</td>
<td>-0.0</td>
<td>-3.0</td>
<td>0.0025</td>
</tr>
<tr>
<td>Intercept</td>
<td>5246</td>
<td>936</td>
<td>5.6</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

R² = 0.06.
KEY MESSAGES

- Low birthweight and impaired fetal growth have been associated with various adult disease manifestations and increased cardiovascular mortality in epidemiological studies from different populations.
- Neuropsychological development may be negatively influenced by reduced fetal growth, with one possible consequence being impaired cognitive function and increased stress susceptibility in adolescence and adult life.
- We examined 90,651 Swedish conscripts for associations between birthweight, adjusted for other birth variables, and scores from a psychological assessment including an evaluation of stress susceptibility.
- Assessment scores for psychological functioning continuously improved up to a birthweight of 4200 g, followed by a decreasing trend above this birthweight level.
- Impaired fetal growth seems to influence not only cognitive function, which has been shown before, but also assessed susceptibility to stress—a factor of possible importance for adverse cardiovascular reactions with long-term detrimental effects.

References


30 Kuopilöva I, Leon DA, Vägerö D. Can confounding by sociodemographic and behavioural factors explain the association between size at birth and blood pressure at age 50 in Sweden? *J Epidemiol Community Health* 1997;51:14–18.