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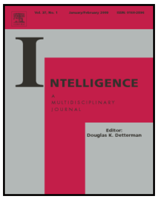

Birth weight and cognitive ability in adulthood: A systematic review and meta-analysis

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ABSTRACT

Birth weight is associated with a range of adult health outcomes. In childhood, there is a positive association between birth weight – in the normal range ($>$2500 g) – and cognitive ability, but no systematic review has yet assessed this effect across adult life. We aimed to synthesise published studies assessing the relationship between birth weight and general cognitive ability in non-clinical adult populations ($\geq$18 years). Nineteen studies ($N =$ 1.122,858), mean participant age ranged from 18 to 78.4 years, fulfilled the inclusion criteria, of which eight could be included in a random-effects meta-analysis. Birth weight was associated with cognitive ability in adulthood, with each kilogram increase in birth weight associated with a 0.13 SD increase in general or fluid intelligence (95% CI [0.07, 0.19]). There was considerable heterogeneity in the effect size ($I^2 = 97.8\%$, 95% CI [97.2, 98.4], $p < 0.001$). The association was similar after correcting for gestational age and parental social class where data were available. The effect size was larger for participants aged $<$60 years than those aged 60 years or over. There is a modest association between birth weight and cognitive ability in adulthood that may diminish at older ages.

1. Introduction

Lower birth weight is associated with adverse outcomes across the lifespan. The concept of the 'Developmental Origins of Health and Disease' (Barker, 2004) has suggested that factors which influence the prenatal environment may also influence health outcomes in adult life. These include somatic outcomes such as infant mortality (Wardlaw, Blanc, Zupan, & Ahman, 2004), all-cause adult mortality (Baker, Olsen, & Sørensen, 2008), cardiovascular disease (Barker et al., 1993; Stein et al., 1996), stroke (Eriksson, Forsen, Tuomilehto, Osmond, & Barker, 2000), and type 2 diabetes (Eriksson, Forsen, Osmond, & Barker, 2003). This relationship extends to neuropsychological outcomes, where lower birth weight has been associated with outcomes such as schizophrenia (Abel et al., 2010), depression (de Mola, de França, de Avila Quevedo, & Horta, 2014; Wojcik, Lee, Colman, Hardy, & Hotopf, 2013), and cognitive ability in childhood (Shenkin, Starr, & Deary, 2004). Birth weight, especially when corrected for gestational age, is a useful marker of prenatal development, and can be influenced by placental insufficiency, maternal malnutrition, lower parental social class, genetic and epigenetic factors, and increased altitude of birth (Feil & Fraga, 2012; Jensen & Moore, 1997; Kramer, 1987).

Low birth weight (LBW $<$ 2500 g) babies have poorer outcomes physically and cognitively than normal birth weight (NBW) controls (Hack, Klein, & Taylor, 1995): a recent meta-analysis identified an association between LBW and poorer cognitive performance in adolescence and young adulthood, with NBW adolescents and adults scoring 7.63 IQ points higher than low birth weight participants (95% [5.95, 9.31]), reduced to 4.98 IQ points after adjusting for publication bias (95% CI [3.20, 6.77]) (Kormos, Wilkinson, Davey, & Cunningham, 2014), with the effect size reducing with increasing age. Some studies have investigated the association between birth weight in the normal range ($\geq$2500 g) and cognitive ability in childhood (see review in Shenkin et al., 2004; Heinonen et al., 2008; Lawlor et al., 2005; Lawlor et al., 2006; Yang, Lynch, Susser, & Lawlor, 2008). There is some evidence that IQ may decline at the highest birthweights ($>$4.5 kg) (Shenkin et al., 2004). The positive association between birth weight in the normal range and cognitive ability in childhood was small: e.g. 0.81 IQ points per SD of birth weight z score adjusted for age and gender at age 5 to 6; 1.30 at age 7 to 9, and 1.44 at age 11 to 12, attenuating to 0.28, 0.67 and 0.52 points after adjusting for family characteristics (Lawlor et al., 2006; Yang, Lynch, Susser, & Lawlor, 2008). The effect is negligible at the individual level, but could have an impact at a population level, and has been a driver for assessing the impact of improving maternal

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health and the impact of socioeconomic influences on long term outcomes. However, observational data cannot be used to recommend interventions to increase birth weight, as there could be unintended consequences: e.g. increasing fetal weight could increase the risk of complications of labour.

Cognitive ability is generally very stable across the lifespan, in the absence of pathology. For example, Deary, Whalley, Lemmon, Crawford, and Starr (2000) identified a correlation of 0.63 between Moray House Test scores at age 11 and 77 years, and 0.73 after adjusting for the sample's ability range. Similarly, the stability coefficient for general intelligence in a cohort of Swedish men was 0.95 between 18 and 50 years, and 0.86 between 18 and 65 years (Rönnlund, Sundström, & Nilsson, 2015). As suggested by the authors, this stability fits well with the parieto-frontal integration theory (P-FIT; Jung & Haier, 2007), which links cognitive stability with neural stability, and cognitive decline to decreased neural stability in old age. Factors from early life can persist into old age, although it has been debated whether this is due to permanent programming in early life or an ageing-related accumulation of deficits (e.g. Kirkwood & Melov, 2011; Walker, 2011). Proponents of permanent programming theories stress that even small differences in early life conditions can influence later health outcomes (Gavrilov & Gavrilova, 2004). The stability of cognitive ability across the lifespan highlights the importance of determining the relationship between early-life factors and cognitive ability in adulthood.

No systematic review has yet assessed the relationship between birth weight and cognitive ability across the entirety of adulthood and across the entire range of birth weight, to assess if the association found in childhood persists, strengthens or weakens.

We aimed to conduct a systematic review and meta-analysis on studies that assessed the relationship between birth weight across the normal range and performance on any cognitive assessment in a non-clinical adult population.

2. Methods

2.1. Protocol and registration

We registered the protocol for this review with the International Prospective Register of Systematic Reviews (PROSPERO) prior to the formal search. Permanent link: http://dx.doi.org/10.15124/CRD42015020380.

2.2. Eligibility criteria

Eligible studies assessed adult participants ($M_{age} \geq 18$ years) of normal birth weight on at least one cognitive test. We considered all observational study types for inclusion. We excluded studies if participants were members of, or matched controls for, a clinical population or a LBW group (<2500 g). We also excluded studies where cognitive ability was only assessed by a measure of cognitive success (e.g. education, employment). We did not limit publications on language or publication date. Studies in which a standardised beta coefficient was provided for the relationship between birth weight and a measure of fluid or general intelligence were included in the meta-analysis. If this was not published in the paper, we contacted the study author.

2.3. Identification of studies

2.3.1. Information sources

We ran an electronic search via OvidSP in EMBASE, PsycINFO and Medline (including in-process and non-indexed citations) in September 2015. We conducted a forward citation search on all studies identified for inclusion in the systematic review, and checked the reference lists of included studies for any further relevant articles.

2.3.2. Search

The search was devised with an experienced librarian, and adapted for each database. Briefly: titles, abstracts and subject headings were searched for terms relating to birth weight AND cognition. (Supplement 1). Animal studies, and studies only including children, were excluded from the search.

2.3.3. Study selection

One reviewer (BJG) screened all titles and abstracts against the eligibility criteria. A second reviewer (JSL) independently reviewed a subset of these studies. Any areas of uncertainty resolved via discussion with CRG or SDS. When studies were from the same cohort we planned to use the paper with the most comprehensive (and recent) data.

2.3.4. Data extraction

The data extraction form was based on the Cochrane Consumers and Communication Review Group's template (CCCRG, 2009), and revised following piloting (Supplement 2). One reviewer (BJG) conducted data extraction, and a second reviewer (YCH) checked all data extracted. Any disagreements were resolved after discussion with CRG or SDS. If the paper did not contain the relevant analysis for inclusion in the meta-analysis, but included a fluid or general cognitive measure, we attempted to contact the corresponding author for further information. We requested the standardised beta coefficient for the relationship between birth weight (per kilogram increase) and standardised fluid ability score, unadjusted, adjusted for gestational age (where possible) and adjusted for both gestational age and a measure of socioeconomic status at birth (where possible).

2.3.5. Risk of bias

Risk of bias was assessed by use of an adapted version of the Quality in Prognostic Studies (QUIPS) tool (Hayden, van der Windt, Cartwright, Côté, & Bombardier, 2013) and was conducted by one reviewer (BJG).

2.4. Results

2.4.1. Meta-analysis

Where data were available, we used meta-analysis, conducted with STATA version 13 (StataCorp 2013), to obtain an overall estimate for the effect and to quantify the estimate's uncertainty. A meta-analysis was conducted for the crude association between birth weight (per kilogram increase) and standardised fluid cognitive ability score. We used DerSimonian and Laird random effect models to calculate the pooled effect for each cohort, which accounts for between-sample variation (Deeks, Altman, & Bradburn, 2001). We examined the heterogeneity of the estimates between studies using the I^2 statistic (with 95% confidence intervals). This statistic quantifies the percentage of total variation across studies due to heterogeneity rather than chance. An I^2 statistic of 25%, 50% or 75% suggests low, moderate or high heterogeneity respectively (Higgins, Thompson, Deeks, & Altman, 2003). We produced forest plots for the overall unadjusted effect. We also examined, through additional meta-analyses, how the effect would change when correcting for gestational age and both gestational age and socioeconomic status at birth. Finally, we conducted subgroup meta-analyses to quantify the effect for different participant age brackets. We assessed risk of publication bias through a funnel plot of studies included in the meta-analysis.

2.4.2. Studies not included in meta-analysis

For studies that did not provide the data required for inclusion in the meta-analysis, but contained relevant information, the results were described in more detail. As we aimed to assess how the effect might change over different stages of life, we presented studies in order of increasing participant age, stratified into different age brackets.

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