Journal of Anxiety Disorders 25 (2011) 1060–1067

Contents lists available at ScienceDirect

Journal of Anxiety Disorders

The association between birth weight and anxiety disorders in young adults

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ARTICLE INFO

Article history:
Received 23 March 2011
Accepted 4 July 2011

Keywords:
Stress disorders
Post-traumatic
Anxiety disorders
Developmental origins
Birth cohort

ABSTRACT

Recent evidence has linked birth weight to later behaviour/mental disorders, yet studies have hitherto neglected to investigate the relationship between birth weight and adult anxiety disorders. Prospectively collected data from 2210 mother/offspring pairs of the Mater University Study of Pregnancy (MUSP) birth cohort was used to test for associations between birth weight *z*-score and four major groupings of DSM-IV anxiety disorders. Birth weight *z*-score was linearly and inversely associated with lifetime diagnosis of post-traumatic stress disorders at 21 years, with those falling within the smallest birth weight quintile group at almost two-fold increased odds (OR = 1.96, 95% CI: 1.10, 3.52) of being diagnosed with the disorder compared to those falling within the largest group. The association remained when subsequent analysis restricted the sample to those exposed to trauma. This is the first study in which birth weight has been found to be associated with post-traumatic stress disorders in adults.

1. Introduction

Evidence from a range of scientific disciplines show that organisms are capable of responding to environmental cues during a critical period of development in an attempt to adapt characteristics better suited to environmental conditions, a process which in humans results in permanent changes that may have pathological consequences in later life (Bateson et al., 2004). Due to the pioneering work of Barker (2004), this has come to be known as the developmental origins of adult disease. The findings presented in numerous reviews across a number of disciplines provide evidence linking altered fetal development to later adult diseases including cardiovascular disease, hypertension, obesity and diabetes type 2 (Warner & Ozanne, 2010). Despite this, few studies have tested the potential role that altered fetal development may have on the later development of mental health disorders.

The majority (Alati et al., 2007; Cheung, Khoo, Karlberg, & Machin, 2002; Gale & Martyn, 2004; Herva et al., 2008; Nomura et al., 2007; Patton, Coffey, Carlin, Olsson, & Morley, 2004; Raikkonen et al., 2007; Wiles, Peters, Leon, & Lewis, 2005), though not all (Osler, Nordentoft, & Andersen, 2005; Vasiliadis, Gilman, & Buka, 2008) of the studies which have tested the relationship between birth weight and mental health symptoms have found small but robust associations with symptoms of distress (Cheung et al., 2002; Raikkonen et al., 2007; Wiles et al., 2005), depression (Alati et al., 2007; Gale & Martyn, 2004; Herva et al., 2008; Patton et al., 2004) and/or anxiety (Nomura et al., 2007). Studies exploring broader behavioural outcomes have found associations between birth weight and stress susceptibility (Nilsson, Nyberg, & Ostergren, 2001) and depressive and anxious symptoms (Alati et al., 2009; Hack et al., 2004, 2009). There is also evidence of no associations (Wiles et al., 2006), and effect modification due to socio-economic factors (Kelly, Nazroo, McMunn, Boreham, & Marmot, 2001). Additional inconsistencies include the nature of the trend, with some reporting inverse, linear associations (Alati et al., 2007; Cheung et al., 2002; Gale & Martyn, 2004; Kelly et al., 2001; Nomura et al., 2007) and others reporting non-linear, reverse J-shaped associations (Alati et al., 2009; Nilsson et al., 2001). Finally, some studies report that birth weight is predictive of later behaviour/mental health problems in females only (Alati et al., 2007; Hack et al., 2004, 2009).

Despite the existing research into the developmental origins hypothesis, the association of birth weight with adult anxiety disorder diagnosis has yet to be tested using data from a birth cohort. In two earlier studies using the Mater University Study of Pregnancy (MUSP) cohort, we found associations between birth weight and anxious/depressive symptoms at child age 14 (Alati et al., 2009) and depressive symptoms in female offspring at age 21 (Alati et al.,

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doi:10.1016/j.janxdis.2011.07.002

2007). The present study aimed to test associations between birth weight and four DSM-IV anxiety disorders, specifically Generalised Anxiety Disorders (GAD), phobias, Panic Disorders (PD), and Post-Traumatic Stress Disorders (PTSD) in young adults.

2. Materials and methods

2.1. Participants

The sampling frame of the MUSP included all pregnant public patients attending consecutive obstetric clinic visits at the Mater Misericordiae Hospital (MMH) in Brisbane between 1981 and 1984. Admission on the grounds of attending a public consultation led to a sample skewed to lower income women, greater detail on the MUSP research design, participants and data collection phases have been described in detail elsewhere (Najman et al., 2005). At baseline, the sample for this study consisted of 6433 Caucasian women and their offspring (52% male). This study restricted all analysis to the Caucasian group, as ethnicity was associated with birth weight, and the need to adjust for the small numbers of non-Caucasians (5% of the 21 year sample) was more easily addressed by exclusion. At age 21 there were 2210 mothers and their offspring with complete data on all variables of interest.

2.2. Measurement of anxiety disorders

Anxiety disorders were measured at the 21 year follow-up using the lifetime version of the Composite International Diagnostic Interview (CIDI-Auto) version 2.1 (World Health Organisation, 1997). The CIDI-Auto is a computerised instrument which was administered by a trained interviewer, and has good validity and inter-rater and test-retest reliability (Peters, Clark, & Carroll, 1998). Anxiety disorders were diagnosed according to the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) (First and Tasman, 2004), for the following selected disorders; Panic Disorders (PD), phobias, Generalised Anxiety Disorders (GAD), and Post-Traumatic Stress Disorders (PTSD). To gain a diagnosis of PTSD participants had to nominate one or more of the eleven possible traumatic events included in the CIDI as having occurred to them in their life time. We combined all trauma events and created two binary variables: life time trauma exposure and 12 month trauma exposure (both coded yes/no). Twelve month and life time diagnoses were made for each of the 2563 (35%) individuals who completed the CIDI-Auto using standard computer algorithms. An age at onset was also elicited from those who met the criteria for these mental disorders.

2.3. Predictors and confounders

Birth weight, gender and gestational age in weeks (GA) were extracted from hospital obstetric records at the time the child was born. As in previous papers (Alati et al., 2007, 2009), fetal growth rate was estimated by calculating birth weight *z*-scores, internally adjusted for gender and GA. The *z*-score was calculated by subtracting from an individual's birth weight, the mean birth weight from all other participants with the same GA and gender, and then dividing by the birth weight standard deviation specific to those with the same GA and gender. In this study, the *z*-score was used both as a continuous variable and split into quintile groups so that the odds of being diagnosed with an anxiety disorder could be observed in each quintile group compared to a reference quintile group (quintile group 1 = smallest *z*-score group, quintile group 5 = highest *z*-score group).

At the first antenatal clinic visit (FCV) maternal smoking was recorded (non-smoker, smoker, heavy smoker) along with maternal alcohol use (abstainer, 0–0.5 drinks/day, 0.5–1.0 drinks/day, >1 drinks/day) during pregnancy. At this time, the Delusions-States-Symptoms Inventory (DSSI) (Bedford & Folds, 1977) assessed maternal antenatal anxiety symptoms (non-anxious, anxious). The DSSI anxiety subscale consists of seven items constructed to include the primary features of an anxiety disorder. The DSSI has been found to correlate well with other established symptoms scales, such as the Edinburgh Postnatal Depression Scale (EPDS) and the Hospital Anxiety/Depression Scale (HADS) (Bedford & Deary, 1999).

At birth, maternal age (13–19, 20–34, ≥35) and parity (0, 1–2, ≥3) were taken, along with the infants' birth weight and gestational age. Concurrent measures of offspring socio-economic position (SEP) were taken at the 21 year follow-up which included offspring income (low, middle, high) and offspring work type (non-manual, manual, student, other/unemployed), along with offspring cigarette use per day (none, 1–19, ≥20) at 21, included as a lifestyle indicator.

2.4. Statistical analysis

All analyses were carried out on a total of 2210 Caucasian mothers and their offspring, all of which had complete data on all measures of interest. Three Phobias including agoraphobias, social phobias and specific phobias were combined into one group (phobias). Logistic regression was used to determine the univariable associations of the birth weight *z*-score quintile groups with both life time and 12 month diagnosis of the four anxiety disorder categories and also to explore the univariable associations between the DSM-IV lifetime disorders and possible confounding factors.

Multivariable logistic regression analysis included adjustment for maternal factors during pregnancy: smoking and alcohol consumption, maternal antenatal anxiety which has been found to be related with both lower birth weight and pre-term delivery (Pritchard & Teo, 1994) and offspring behavioural/mental health problems (O'Connor, Heron, Golding, & Glover, 2003), maternal age at birth and parity. Concurrent measures of offspring SEP and lifestyle, such as income, work type patterns and smoking status were also included in the fully adjusted model. As we found birth weight was associated with a diagnosis of PTSD, which requires exposure to a traumatic event, we conducted additional analyses. Firstly we investigated whether birth weight was associated with trauma exposure. Then, we restricted the sample to those exposed to trauma ($n = 1136$) by excluding those who did not report experiencing a traumatic event. We repeated univariable and multivariable logistic regression analyses to investigate whether birth weight predicted PTSD diagnosis among trauma exposed participants odds ratios and 95% confidence intervals (95% CI) are presented for the unadjusted and fully adjusted models.

For disorders which were found to be associated with birth weight, gender was tested as an effect modifier. We also conducted unadjusted and adjusted Cox regression analysis to estimate hazard ratios (HR) of receiving an anxiety disorder diagnosis with 95% CI. We used likelihood ratio tests to test for linearity (by entering birth weight *z*-score into all models as a continuous variable), and quadratic terms to test for non-linear associations. All analyses were conducted using STATA 11 (STATA Corp LP).

2.5. Adjustment for attrition

The participants in the analysis represented 35% of the original cohort restricted to Caucasian participants ($n = 6433$). In order to determine if differential loss to follow-up was likely to have biased the results of the study, we fitted a multivariate logistic regression model to compare a number of baseline factors between those who were still in the study and those that were lost to follow-up.

Starting from a missing at random (MAR) assumption (Sterne et al., 2009) we used the STATA procedure of multiple imputation,