



Perinatal maternal life events and psychotic experiences in children at twelve years in a birth cohort study[☆]



Sarah Dorrington^{a,*}, Stan Zammit^{b,d}, Laura Asher^c, Jonathan Evans^a, Jonathan Heron^b, Glyn Lewis^e

^a Department of Psychological Medicine, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom

^b School of Social and Community Medicine, Oakfield House, Oakfield Grove, Bristol BS8 2BN, United Kingdom

^c Centre for Global Mental Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT, United Kingdom

^d Department of Psychological Medicine & Neurology, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Heath Park, Cardiff CF14 4XN, United Kingdom

^e Mental Health Sciences Unit, Faculty of Brain Sciences, University College London, W1W 7EJ, United Kingdom

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ABSTRACT

Background: International studies indicate that the median prevalence of psychotic experiences in children is 7%. It has been proposed that environmental stress during pregnancy may affect the neurodevelopment of the foetus and lead to a vulnerability in the child to later stressors and psychopathology.

Aim: In this study we explore the relationship between environmental stress during pregnancy and psychotic experiences in children in the general population at 12 years.

Methods: We analysed a birth cohort of 5038 children from the Avon Longitudinal Study of Parents and Children. Environmental stress was measured as life event exposure. Data on life events were collected on women during their pregnancy, whilst psychotic experiences in the offspring were assessed at age 12.

Results: There was a weak association between maternal exposure to life events and psychotic experiences at twelve years (crude OR 1.10 95% CI 1.02–1.18) per quartile of life event score. This association was not reduced after adjustment for socio-economic status, family history of schizophrenia, maternal education or birth weight but after adjustment for maternal anxiety and depression and smoking in early pregnancy there was no longer any evidence for an association (OR 1.01 95% CI 0.93–1.10).

Conclusion: This study provides some evidence to suggest that stressful life events may affect child psychotic experiences through effects on maternal psychopathology, and possibly physiology, during pregnancy.

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1. Introduction

It has been proposed that environmental stress, during pregnancy, such as life event exposure, may affect the neurodevelopment of the foetus and lead to an increased risk of psychopathology (Lou et al., 1994; Walker and Diforio, 1997; van Os and Selten, 1998; Araya et al., 2009; Kinsella and Monk, 2009).

Studies looking at the effects of stress on foetal development suggest that glucocorticoids play a role in both early neurodevelopment and later atrophic processes which may be involved in the development of a range of psychopathology (Cotter and Pariante, 2002), including psychotic experiences in childhood. Neurodevelopmental studies

have found that prenatal environment can alter behaviour and neuroendocrine systems, and affect the hippocampal structure of primates (Coe et al., 2003). Reduced hippocampal formation (Weinberger, 1999) and variation in pituitary volume (Garner et al., 2009) have also been seen throughout the progression of schizophrenia in humans.

Several studies propose that these alterations in the hypothalamic–pituitary–adrenal (HPA) axis (Gitau et al., 1998; Kaplan et al., 2008; O'Donnell et al., 2009) and alterations in placental enzymes (Gluckman et al., 1999) caused by environmental stress may affect the neurodevelopment of the foetus (Coe et al., 2003) and have significant later effects on the child (Talge et al., 2007). Walker and Diforio's (1997) neural diathesis stress model of schizophrenia incorporates prenatal factors and the augmentation of dopamine and dopamine receptor synthesis by the HPA axis (Walker and Diforio, 1997). Longitudinal studies are required to examine effects of prenatal stressors on risk of schizophrenia whilst minimizing recall bias, but are rarely feasible given the incidence of this disorder. However, psychotic experiences during childhood are relatively common in the general population and offer the potential for using cohort studies to examine the aetiology of psychosis. In the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort, definite psychotic experiences were present in approximately 5% of children aged 12 years (Horwood et al., 2008).

Abbreviation: HPA, hypothalamic–pituitary–adrenal axis.

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* Corresponding author at: 9a Nettleton Road, New Cross Gate, London SE14 5UJ, United Kingdom. Tel.: +44 7846241211.

E-mail addresses: sarah.dorrington@kcl.ac.uk (S. Dorrington), zammits@cardiff.ac.uk (S. Zammit), laura.asher@lshtm.ac.uk (L. Asher), jonathan.evans@bristol.ac.uk (J. Evans), jonathan.heron@bristol.ac.uk (J. Heron), glyn.lewis@bristol.ac.uk (G. Lewis).

This finding is consistent with findings from a recent systematic review and meta-analysis that reported the median prevalence of psychotic experiences as 7% (Linscott and van Os, 2012). Although it is not clear to what extent psychotic experiences reflect pathology underlying disorders such as schizophrenia, and the majority of such experiences in childhood remit (Escher et al., 2002; van Os et al., 2009; De Leede-Smith and Barkus, 2013), nevertheless children with psychotic experiences are at increased risk of developing schizophreniform disorder (Poulton et al., 2000) and other psychotic disorders (van Os et al., 2009; Werbeloff et al., 2012; Zammit et al., 2013) in later life.

Although Spauwen et al. reported an association between psychotic experiences in children and antenatal life events (Spauwen et al., 2004), this relationship has not been adequately explored. In their study of 963 adolescents, children exposed to antenatal or pregnancy-related stress had increased odds of reporting psychotic experiences in adolescence, but the main limitation of this study was that data was retrospective, and therefore results may have been affected by maternal recall bias.

The aim of this study is to determine, using longitudinal data, if there is an association between perinatal environmental stressors, measured as life event exposure during pregnancy, and psychotic experiences at twelve years in a birth cohort study.

2. Methodology

2.1. Sample

Data were drawn from the Avon Longitudinal Study of Parents and Children (ALSPAC), an ongoing population-based study designed to investigate the effects of a wide range of influences on the health and development of children. Pregnant women residing in the south-west of England who had an estimated date of delivery between April 1, 1991 and December 31, 1992 were invited to participate. The initial study cohort consisted of 14,062 pregnancies and 13,978 (52% boys and 48% girls) singletons/twins still alive at 12 months of age.

Parents have completed regular postal questionnaires concerning their child's health and development since birth. Since 7.5 years of age, the children attended annual assessment clinics where they participated in face-to-face interviews. In this study, lower social class families, parents with lower education, male children and minority ethnic status participants were more likely to be non-attenders (Horwood et al., 2008).

Compared to the 1991 UK National Census Data, the ALSPAC sample showed a slightly higher proportion of house owner-occupiers and a smaller proportion of mothers from ethnic minorities (Golding et al., 2001). As described in Boyd et al. (2013), children enrolled in ALSPAC were more educated at 16 compared to the national average, were more likely to be white (reflecting the ethnical composition of the area from which the sample was drawn) and less likely to be eligible for free school meals (an indicator of low income in the UK). Detailed information about ALSPAC is available online (<http://www.bris.ac.uk/alspac>). Please note that the study website contains details of all the data that is available through a fully searchable data dictionary.

The 'psychotic symptoms in childhood semi-structured interview' (Horwood et al., 2008), was conducted when children were 12 years of age.

2.2. Measures

2.2.1. Outcomes

The interview for psychotic experiences in childhood consists of 12 core questions covering the last 6 months. Questions include visual and auditory hallucinations; delusions of being spied on, persecution, thoughts being read, reference, control, grandiose ability and other unspecified delusions; and experiences of thought interference such as thought broadcasting, insertion and withdrawal. For these 12 core items, 7 screening questions were derived from DISC-IV (Shaffer et al.,

2000) and 5 questions from the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) version 2.0, modified slightly after piloting. Clinical cross-questioning and probing were used to establish the presence of psychotic experiences, and coding of all items followed the glossary definitions and rating rules for SCAN. Interviewers were psychologists trained in using the psychotic experiences in childhood interview. Psychotic experiences were rated as either not present, suspected or definitely present. Psychotic experiences were only rated as definite when a credible example was provided and unclear responses were always 'rated down'. Psychotic experiences were included in our analyses if they were not attributable to effects of sleep, fever or substance use. This is consistent with the approach of classification systems for diagnosis of functional psychotic disorders. The average kappa value for interrater reliability was 0.72 (Horwood et al., 2008).

We examined two childhood outcomes:

- 1) Presence or absence of any suspected or definite psychotic experiences (prevalence 13.2% in total sample at 12 years)
- 2) A narrower outcome of definite psychotic experiences only (prevalence 5.6% in total sample at 12 years)

2.2.2. Exposures

Data on life events (SLEs) were obtained from a maternal questionnaire delivered at two time points. The sources for the life event questionnaire were the work of Brown et al. (1973a) and Barnett et al. (1983). The questionnaire includes a life-event inventory, which was derived for the present study using previous inventories as a basis for selection of items. Each life event had 5 response categories indicating not only whether or not the event occurred but also to what extent the respondent was affected by it. The early pregnancy questionnaire was given to pregnant mothers at 18 weeks following last menstrual period (LMP). This specifically asked about events in early pregnancy. The late pregnancy questionnaire was given to the same mothers at 8 weeks into the postnatal period. This asked specifically about life events in late pregnancy and postnatally. In addition to our primary analysis we will look at life event data from the early and late pregnancy questionnaires separately. Of completed questionnaires, 40% of early and late pregnancy questionnaires were completed at the specified time points (18 weeks gestation and 8 weeks postnatal). 90% of early pregnancy questionnaires were completed by 25 weeks gestation. 90% of late pregnancy questionnaires were completed by 12 weeks since delivery. 97.1% of mothers who completed the early pregnancy questionnaire completed it by 40 weeks after their LMP (by which time 73.8% of mothers had given birth). This questionnaire is much more specific to pregnancy than the late pregnancy questionnaire. The late pregnancy questionnaire predominantly covers the second half of pregnancy as well as the immediate postnatal period.

If a life event had not occurred then it was scored as 0. For each life event recorded as having occurred, mothers gave the event a subjective scoring from 'not affected at all' (1) to 'severely affected' (4). In order to take into account the wide variation of severity of life events, and the limited (1–4) subjective ratings, we weighted the life events which affected mothers most severely.

2.3. Confounders

Various sociodemographic variables were considered as potential confounders: parental social class (highest of both parents, based on occupation using the 1991 Office for Population Censuses and Surveys classification); gender; and maternal education (four levels ranging from the lowest UK school-leaving qualifications to degree level). We also examined single parenthood; father's age at conception; family history of schizophrenia (in parents and grandparents), family history of depression (in parents and grandparents), maternal history of severe depression, pregnancy complications (gestational diabetes or maternal hypertension) and birth weight as potential confounders. We looked

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