



## Research paper

## The impact of pre- and perinatal factors on psychopathology in adulthood

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## ABSTRACT

**Background:** : There is considerable evidence that pre- and post-natal factors are associated with a wide range of psychopathology in offspring during childhood and adolescence.

**Objective:** : The main aims of the present study were to examine the associations between pre- and perinatal factors and psychopathology in offspring during adulthood, and to explore whether family factors (i.e., family cohesion, mother's social support, and father's social support) mediate these relationships.

**Method:** : Information on pre- and perinatal events was collected from biological mothers of the participants ( $N = 315$ ) when they were between 14 and 18 years who were then followed up until they reached age 30.

**Results:** : Maternal obstetric history and illness during first year were significant predictors of offspring anxiety disorder. Maternal emotional health predicted offspring affective disorder. Difficult delivery and breast feeding predicted disruptive disorder. The relationship between maternal obstetric history/emotional health and anxiety/affective disorder was no longer significant after controlling for family cohesion.

**Limitations:** : The information was based on maternal recall when their offspring were between 14 and 18 years which may be subjected to recall bias.

**Conclusion:** : The association between pre- and postnatal factors and psychopathology of offspring during adulthood is mediated by familial factors.

## 1. Introduction

Research during the past three decades has provided considerable evidence that pre- and postnatal factors are associated with a wide range of psychopathology during childhood and adolescence (Allen et al., 1998; O'Connor et al., 2002, 2003; Stene-Larsen et al., 2009; Taylor et al., 2017). Pre- and postnatal factors can be grouped under (1) prenatal environment (e.g., maternal physical and mental health, experiences of stress during the pregnancy, and use of drugs during pregnancy); (2) intrapartum events (e.g., surgical delivery and birth difficulties); (3) early neonatal environment (e.g., prematurity and anoxia); and (4) later neonatal environment (e.g., breast feeding and infant health during the first year of life) (Allen et al., 1998).

Amongst the prenatal environments, maternal anxiety or depression has consistently been linked with behavioral and/or emotional problems in the offspring (O'Connor et al., 2002). As reported in a series of studies conducted by O'Connor et al. (2002, 2003), women with a high level of anxiety at 32 weeks' gestation had double the risk of having children with behavioral problems at 4 and 7 years of age; children from this group of women also had high risk of having attention-deficit/

hyperactivity disorder (ADHD), anxiety or depression, or conduct disorder symptoms; the attributable load in behavioral problems that are due to antenatal anxiety was estimated to be 15%. A recent study by Korhonen et al. (2012) showed maternal prenatal depression to be associated with adolescent boys' (but not girls) poor psychosocial functioning and with externalizing problems.

Maternal smoking during pregnancy is another prenatal event that has consistently been linked with an increased risk of externalizing behaviors such as ADHD and conduct disorder among offspring (Indredavik et al., 2006; Nigg et al., 2007; Stene-Larsen et al., 2009; Schmitz et al., 2006; Wakschlag et al., 2006). Taylor et al. (2017) recently compared the associations of maternal smoking during pregnancy and mother's partner's smoking during pregnancy with offspring depression using four large data sets from the UK, Sweden, Brazil, and Norway. Maternal smoking during pregnancy was associated with an increased risk of offspring depression, but not with paternal smoking during pregnancy. Interestingly, individuals whose mothers smoked during pregnancy, compared to their siblings from another pregnancy in which the mother did not smoke, were no more likely to have depression; the authors suggested that the association between maternal

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smoking during pregnancy and offspring depression may have been confounded by unmeasured factors.

Intrapartum events such as obstetrical complications are significantly higher among individuals with a wide range of psychiatric disorders compared with those without any psychiatric disorders (Cantor-Graae et al., 1993; Kinney et al., 1994; see review by Serati et al., 2017). For example, in a study by Done et al. (1991) patients with mood disorder had significantly higher rates of obstetrical complications than participants from the general population. Xu et al. (2007) examined whether there is link between obstetrical complication and the presence of depression; their results showed obstetric and prenatal complications to be significantly more frequent among patients with depressive disorder compared to adult siblings without this disorder. In a recent study by Nguyen et al. (2012), women with severe mental illness (i.e., schizophrenia, bipolar, and non-psychotic disorders) were found to have a lower rate of spontaneous vaginal delivery and a higher rate of complications during pregnancy compared to women in the general population. A recent study by Buoli et al. (2016) found 17% of the patients with psychotic and mood disorders to have a history of obstetrical complications.

Early neonatal events such as low birth weight have frequently been reported to be linked with anxiety disorders (Nomura et al., 2007), as well as with anxiety and depressive symptoms (Alati et al., 2009). A recent review by Serati et al. (2017) has identified low birth weight to be a major risk factor for ADHD in children and adolescents. Betts et al. (2011) recently examined the association between birth weight and anxiety disorder in young adults using data from the Mater University Study of Pregnancy. A linear and inverse association was found between birth weight and post-traumatic stress disorder. However, some other studies failed to find any associations between birth weight and mental health problems (Wiles et al., 2006), and others found this association only among females (Alati et al., 2007; Hack et al., 2009).

Late neonatal events, which include breastfeeding, have been associated with emotional and behavioral problems in offspring. Specifically, offspring who were not breastfed compared to those who were breastfed had a higher levels of emotional and behavioral problems, such as anxiety and depression (Allen et al., 1998; Hayatbakhsh et al., 2012; Heikkila et al., 2011; Liu et al., 2014; Oddy et al., 2010; Reynolds et al., 2014), and ADHD (Mimouni-Bloch et al., 2013; Sabuncuoglu et al., 2014; Schmitt and Romanos, 2012; Stadler et al., 2016; Shamberger, 2012). In a more recent study, Loret de Mola et al. (2016) examined the association between breastfeeding and mental health outcomes (i.e., depression, generalized anxiety disorder, social anxiety disorder, and common mental disorders) among young adults in Brazil. Information on breastfeeding was collected in early childhood and the participants were re-interviewed at young adulthood. Participants who were breastfed for more than six months were less likely to have more severe depressive symptoms. Furthermore, a longer duration of breastfeeding was associated with a lower risk of disease. However, findings of studies that examined the role of breastfeeding and children's emotional problems have been inconsistent. For example, Allen et al. (1998) found no significant effect of breast feeding on anxiety and depression in adolescents.

While the above studies have examined specific types of pre- or postnatal factors, Allen et al. (1998) examined the association between a wider range of factors and non-schizophrenic psychopathology in offspring at the age of 18 years. Offspring depression at adolescence was found to be associated with not being breast fed and with maternal emotional problems during the pregnancy, whereas anxiety disorder was associated with fever and illness during late postnatal and with maternal history of miscarriage and stillbirth. Disruptive behavior disorder at adolescence was related to poor maternal emotional health during the pregnancy and with birth complications. Substance use disorders in the offspring were predicted by maternal substance (i.e., alcohol, cigarettes, caffeine, and marijuana) during the pregnancy.

While informative, little is known about the long-term impact (i.e., in adulthood) of pre- and postnatal factors in predicting the development of psychiatric disorders by using data from the same birth cohort. Studies that examined the factors that mediate the association between pre- and postnatal factors and psychopathology are also lacking. Previous studies suggest that familial environment is an important factor in the manifestation of specific pre- and perinatal behavior (e.g., Cernadas et al., 2003), and thus the effects of family cohesion, mother's social support, and father's social support were examined in the present report as potential mediators.

Family cohesion and familial social support are influential factors that have been linked to prenatal maternal stress. For example, Kingston et al. (2012) showed that low family cohesion during childhood was indirectly associated with prenatal stress through current family cohesion and socioeconomic position. In this study, perceived social support also influenced prenatal stress indirectly through socioeconomic position and childhood stress.

Family functioning does not pose a risk only for the pregnant mother but for the offspring as well. Abell et al. (1991) found that women who perceived their families as dysfunctional were delivered of infants with lower birthweight. Pilowsky et al. (2006) showed that family discord factors were associated with both parental and offspring depression. Taken together, it can be hypothesized that prenatal and perinatal factors are influenced by family environment under which the pregnancy progress and these factors are predictive of future psychopathology. However, most studies that have been reported to date are cross-sectional in nature and the mediating effect of familial factors has not been adequately evaluated. Prenatal and perinatal factors occur either spontaneously or are determined by a complex interaction of biological factors; in contrast, the mediating effects of familial environment pose a target for intervention that can benefit the child as well as the mother.

Based on the above background, the present study reports the result of a 16-year longitudinal study on the association between pre- and perinatal factors and psychopathology in offspring at adulthood. The specific aims address the two following questions: (a) What is the association between pre- and perinatal factors and psychopathology in offspring at age 30? The prenatal and perinatal factors examined cover a range of effects during the pregnancy, intrapartum (at birth), and neonatal periods. The types of offspring psychopathology examined were anxiety, affective, disruptive, and substance use disorders. (b) Do specific familial factors (i.e., father and mother social support and family cohesion) mediate the relationship between pre- and perinatal factors and psychopathology in offspring at age 30?

The hypotheses to be tested in this study were as follows: First, based on previous studies in children and adolescents (O'Hara, 1995; Heikkila et al., 2011; Liu et al., 2014; Oddy et al., 2010; Reynolds et al., 2014), pre- and perinatal factors experienced during the pregnancy, intrapartum (birth), and neonatal periods are expected to be associated with psychopathology at age 30. Second, the association between pre- and perinatal factors and adult psychopathology is predicted to be mediated by low levels of family cohesion, as well as by low social support from mother and father (Allen et al., 1998).

## 2. Methods

### 2.1. Participants

The present study used data from the Oregon Adolescent Depression Project (OADP; Lewinsohn et al., 1993), a 16-year longitudinal study of a large cohort of high school students who were randomly selected from nine high schools in western Oregon (Fig. 1). The participants were assessed twice during adolescence, a third time when the average age was 24, and a fourth time when the average age was 30. A total of 1,709 adolescents (ages 14–18; mean age 16.6, SD = 1.2) completed the initial (T1) assessments between 1987 and 1989, with a response rate at

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