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Risk of substance use disorders following prenatal or postnatal exposure to bereavement

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ABSTRACT

Introduction: Substance use disorder (SUD) is associated with major socioeconomic consequences but its etiology is only partly known. The disease predisposition may be established early in life and prenatal stress may play a role. We aimed to examine whether prenatal maternal bereavement, as the indicator of prenatal stress, was associated with an increased risk of SUD in offspring.
Methods: This population-based cohort study included all children born in Denmark ($N = 1\,686\,416$) and Sweden ($N = 2\,563\,659$) from 1973 to 1997. The exposure was maternal bereavement by the death of a close relative 1 year before or during pregnancy. Children were followed from 10 years of age until their death, migration, onset of substance abuse, or December 31st, 2007. The main outcome is hospitalization due to substance use disorder (SUD).
Results: A total of 100 363 children (2.45%) were born to mothers who had experienced bereavement 1 year before or during pregnancy. Overall, these exposed children had a similar risk of hospitalization due to SUD (IRR = 1.02, 95% CI: 0.98–1.07), compared to unexposed children. Children born to mothers who lost a spouse during pregnancy had a two-fold risk (IRR = 2.19, 95% CI: 1.74–2.76) and similar elevated risks were observed in children whose mothers lost a spouse during the first 10 years after child birth.
Conclusions: Our data do not support a programming role of prenatal stress following maternal bereavement on SUD later in life. The increased risk in relation to spousal bereavement may mostly be explained by postpartum changes in familial environment.

1. Introduction

Substance use disorder (SUD) refers to the harmful or hazardous use of psychoactive substances, including alcohol and illicit drugs, which is a major health and social problem worldwide (Barker, 2009; Lowinson et al., 2005). SUD involves a number of behavioral, cognitive, and physiological problems (Burke et al., 2005) and its etiology is complicated and remains to be elucidated (Barker, 2009; Lowinson et al., 2005). Initiation of SUD often occurs during adolescence (Johnston et al., 2011), indicating the importance of early life exposures. Recent evidence suggests that prenatal stress exposure play a programming role in neurological and brain development (Gitau et al., 1998; Talge et al., 2007; Viltart and Vanbesien-Mailliot, 2007; Welberg and Seckl, 2001), which could lead to poor stress management and personality problems (Davis et al., 2011) that may increase the risk of SUB.

Bereavement is a severe life event known to induce both short- and long-term stress (Li et al., 2005; Rubin and Malkinson, 2001). Already, Huttunen and Niskanen (1978) in a case–control design, introduced the idea of using prenatal loss of a father, to estimate the effect of antenatal stress on psychiatric disorders. Recent cohort

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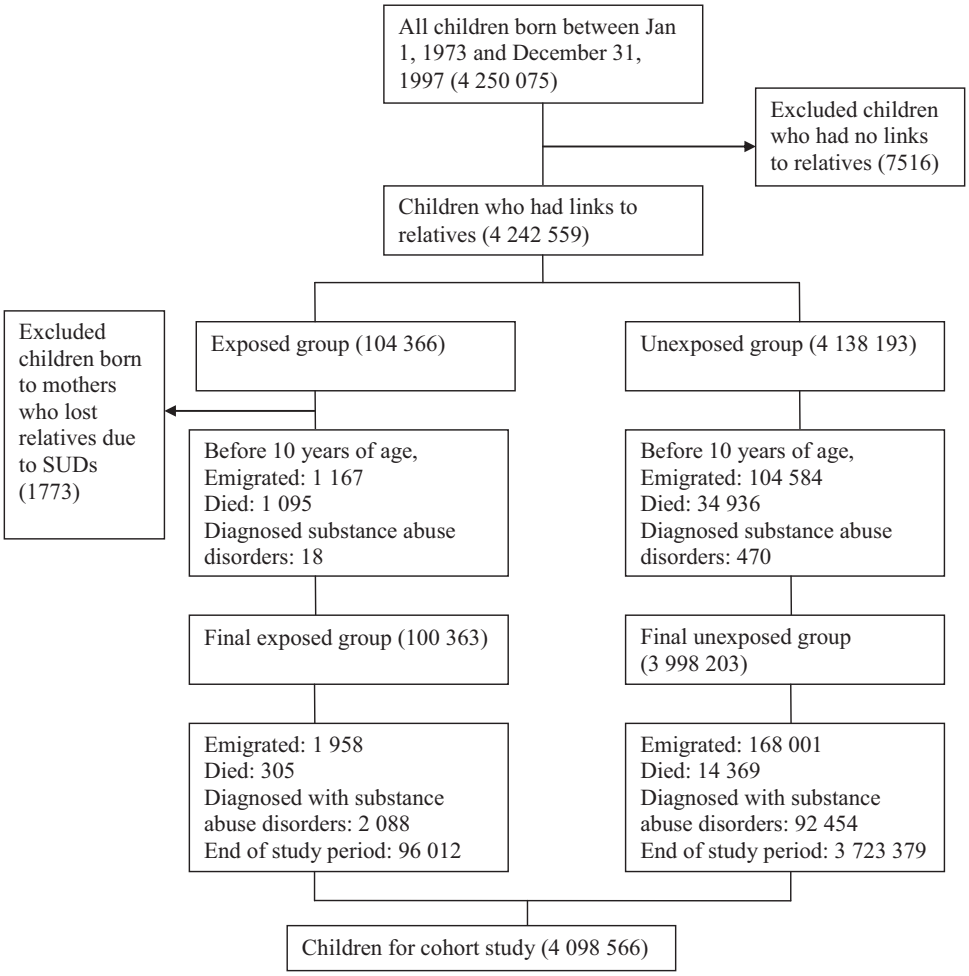

Fig. 1. Flow chart for study population in exposed and unexposed groups.

studies have shown positive associations between prenatal loss of a close relative and selected neurological/behavioral/psychiatric disorders (Khashan et al., 2008, 2011; Li et al., 2009b), but not others (Li et al., 2009a, 2008), suggesting different underlying mechanisms for varied outcomes. Furthermore, the positive associations were based on small numbers of cases (Khashan et al., 2008, 2011; Li et al., 2009b), which lead to the concern of uncertainties in those studies. In addition, the timing of prenatal stress is important for outcomes related to brain development (Kapoor et al., 2006; Sandman et al., 2011) but findings have, however, been inconsistent (Hansen et al., 2000; Khashan et al., 2008, 2011; Li et al., 2011). The role of timing of exposure in the association remains to be elucidated.

We hypothesized that prenatal maternal stress following bereavement could have adverse effects on brain development (Gitau et al., 1998; Talge et al., 2007; Viltart and Vanbesien-Mailliot, 2007; Welberg and Seckl, 2001), leading to an increased risk of behavioral disorders in offspring. In this large population-based cohort study, we aimed to examine the association between prenatal maternal bereavement and the risk of hospital visits due to SUD. We expected that maternal bereavement due to the death of a child or a spouse would be associated with higher risks than the death of other relatives, such as siblings or parents (Beversdorf et al., 2005; Kinney et al., 2008; Li et al., 2005, 2003). We further expected that the timing (Beversdorf et al., 2005; Davis and Sandman, 2010; Khashan et al., 2008, 2011) of exposure may play a role in these associations.

2. Methods

2.1. Study population

The unique personal identification number in Nordic countries permits accurate linkage of data between national registers (Frank, 2000) and we conducted this population-based cohort study based on linked national registers in Denmark and Sweden (Li et al., 2010). Between January 1st 1973 and December 31st 1997, we identified all persons born alive in Denmark (N = 1 686 416) and Sweden (N = 2 563 659) from the Danish and Swedish Civil Registration Systems. Cohort members were followed from 10 years of age until the first diagnosis of substance abuse, death, emigration, or December 31, 2007, whichever came first. Family relatives were identified using the Danish Civil Registry System (Pedersen et al., 2006) and the Swedish Multi-generation Register (Li et al., 2010). Fig. 1 describes the study population. We excluded children whose mothers had no links to any relatives (their father, mother, siblings or spouse, N = 7516), children born to mothers who lost a relative due to SUD (N = 1773), children who emigrated (N = 105 751), died (N = 36 031), and those who had a diagnosis of SUD before 10 years of age (N = 488, mostly likely due to coding errors). At the start of follow-up, our exposed and unexposed cohorts included 100 363 and 3 998 203 children, respectively.

2.2. Exposure and outcome

We categorized children as exposed to prenatal stress if their mothers lost a child, a spouse, a sibling, or a parent within 1 year before pregnancy or during pregnancy. The remaining children were included in the unexposed cohort.

Information on mental and behavioral disorders due to psychoactive substance use for index children was obtained from the Danish Psychiatric Central Register (Munk-Jorgensen and Mortensen, 1997) and the Danish National Hospital Register (Andersen et al., 1999), which holds information on all admissions to inpatients facilities since 1969 and outpatient visits since 1995 in Denmark. Similar information was obtained from the Swedish Hospital Discharge Register, which holds