Social Science & Medicine 97 (2013) 259–266

Contents lists available at SciVerse ScienceDirect

Social Science & Medicine

journal homepage: www.elsevier.com/locate/socscimed

Malnutrition in early life and adult mental health: Evidence from a natural experiment

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ARTICLE INFO

Article history:
Available online 20 December 2012

Keywords:
Famine
Mental health
Selection effect
Natural selection in utero
China
Life course

ABSTRACT

As natural experiments, famines provide a unique opportunity to test the health consequences of nutritional deprivation during the critical period of early life. Using data on 4972 Chinese born between 1956 and 1963 who participated in a large mental health epidemiology survey conducted between 2001 and 2005, we investigated the potential impact of exposure to the 1959–1961 Chinese Famine in utero and during the early postnatal life on adult mental illness. The risk of mental illness was assessed with the 12-item General Health Questionnaire (GHQ-12) and eight other risk factors, and the famine impact on adult mental illness was estimated by difference-in-difference models. Results show that compared with unexposed women born in 1963, women born during the famine years (1959–1961) had *higher* GHQ scores (increased by 0.95 points; CI: 0.26, 1.65) and *increased* risk of mental illness (OR = 2.80; CI: 1.23, 6.39); those born in 1959 were the most affected and had GHQ scores 1.52 points higher (CI: 0.42, 2.63) and an OR for mental illness of 4.99 (CI: 1.68, 14.84). Compared to men in the 1963 birth cohort, men born during the famine had *lower* GHQ scores (decreased by 0.89 points; CI: −1.59, −0.20) and a nonsignificant *decrease* in the risk of mental illness (OR = 0.60; CI: 0.26, 1.40). We speculate that the long-term consequences of early-life famine exposure include both the selection of the hardiest and the enduring deleterious effects of famine on those who survive. The greater biological vulnerability and stronger natural selection in utero of male versus female fetuses during severe famine may result in a stronger selection effect among men than women, obscuring the deleterious impact of famine exposure on the risk of mental illness in men later in life.

Introduction

Child undernutrition remains highly prevalent across the world, in particular in low and middle income countries, where 32% (178 million) of children younger than 5 years had weight-for-age *Z* scores of less than −2 in 2005 according to the new WHO Child Growth Standards (Black et al., 2008; de Onis & Blossner, 2003), which accounted for a third of child deaths and more than 10% of the total global disease burden (Black et al., 2008). Child undernutrition has been increasingly implicated in long-term health and development problems (Barker, 2003; Harper, Susser, St. Clair, & He, 2010; Lumey, Stein, & Susser, 2011; Stein et al., 2007; Victora et al., 2008). In particular, malnutrition during the critical period of brain development of the first 1000 days (pregnancy and the first two years) may also cause permanent deficits in brain and behavioral function (Galler & Barrett, 2001; Galler, Waber, Harrison, & Ramsey, 2005; Levitsky & Strupp, 1995; Venables & Raine, 2012).

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http://dx.doi.org/10.1016/j.socscimed.2012.09.051

As a natural experiment, famine provides a unique opportunity to test the effect of early-life severe nutritional deprivation on a series of adult outcomes including mental (Brown & Susser, 2008; Lumey et al., 2011; Stein, 1975). The earliest evidence suggested that prenatal exposure to the Dutch famine caused by a Nazi blockade of western Holland from 1944 until liberation in May 1945 was associated with an excess of congenital nervous system abnormalities, mainly neural tube defects (Lumey et al., 2011; Stein, 1975). Subsequent studies also suggested that famine exposure in early gestation likely increases adult schizophrenia risk (see a review by Susser, Hoek, & Brown, 1998). Similar associations were observed in the Chinese 1959–1961 famine. Two recent studies based on psychiatric hospital records from different sites reported a two-fold increased risk of schizophrenia among those conceived or in early gestation at the height of famine (St. Clair et al., 2005; Xu et al., 2009). Another study based on the 1987 China National Survey on Disability showed that in urban areas Chinese who were conceived, born, and raised during the famine have a higher risk of schizophrenia than both prefamine and postfamine cohorts. In rural areas, however, the famine cohorts and prefamine cohorts had a lower risk of developing schizophrenia than the postfamine cohorts (Song, Wang, & Hu, 2009), which was interpreted as the result of a more intense survival selection weeding out the frail in rural areas due to the greater severity of the famine in these areas (Song et al., 2009). Research on the Dutch famine has also suggested that early life famine exposure may increase risk of other psychiatric disorders in addition to schizophrenia in adulthood, including antisocial personality disorder (Neugebauer, Hoek, & Susser, 1999; Susser et al., 1998) and major affective disorders (Brown, Susser, Lin, Neugebauer, & Gorman, 1995; Brown, van Os, Driessens, Hoek, & Susser, 2000) as well as general symptomatic measures of mental illness that are not diagnosis-specific among offspring of famine survivors (Stein, Pierik, Verrips, Susser, & Lumey, 2009).

In the present study, we used data from a recent epidemiological survey on mental disorders in China to investigate the potential impact of famine exposure in utero and/or in early postnatal life on the risk of a broad spectrum of mental illnesses in late adulthood. The purposes of this study were twofold. First, we estimated the potential long-term effect of the famine on mental illness among the famine survivors. Second, we tested a hypothesis that the effect of famine on mental disease is not sex-neutral; that is, it is different between men and women.

Our study contributes to the literature in several ways. First, previous Chinese studies replicated the Dutch famine results for schizophrenia, leaving the potential effect of the famine on other mental disorders unexamined in the Chinese context. Famine research in various contexts is crucial for a better isolation of the independent health consequences of famine exposure and consequent nutritional deficiency from alternative mechanisms such as toxic food substitutes, which are more difficult to rule out in any single context (Lumey et al., 2011). Second, extensive literature has suggested a male vulnerability under environmental stress (Catalano et al., 2012; Trivers & Willard, 1973), in particular that famine effects might be different between men and women survivors (Mu & Zhang, 2011). We were especially interested in whether the mental health consequence of famine exposure is sex-specific.

Background

The Chinese Great Leap Forward Famine

The Chinese famine occurring between 1959 and 1961 was one of the worst catastrophes in Chinese history (Ashton, Hill, Piazza, & Zeitz, 1984; Smil, 1999). Although the causes of the famine remain under debate, the weather, specifically a drought, has traditionally been blamed; this notion has been perpetuated by the Chinese, who continue to refer to it as "three years of natural disasters (*san nian zi ran zai hai*)" despite more evidence suggesting that policy failures played a major role (Lin, 1990; Lin & Yang, 2000). In 1958, Mao launched the Great Leap Forward Campaign, during which millions of peasants were mobilized to assist in heavy industry and to promote iron production in particular. In rural areas, mess hall communes were built, and private kitchens were prohibited. Farmers were provided free meals, and tremendous food waste was recorded during the harvest year of 1958 right before the famine (Chang & Wen, 1997; Johnson, 1998; Li & Yang, 2005; Lin & Yang, 2000; Peng, 1987; Yang, 1996; Yang & Su, 1998). Famine suddenly hit China in 1959, and grain output dropped sharply during the next three years. During the worst year—1961—only 70% of the amount produced in 1958 was reached (Chen & Zhou, 2007). Daily consumption per capita decreased dramatically to 1500 calories, far below average energy requirements of 2100 calories per day (Ashton et al., 1984; Chen & Zhou, 2007). Because of the inflexible nature of the centrally planned procurement system, the Chinese government failed to adjust the procurement and transfer of food to thousands of heterogeneous counties as a necessary response to the food shortage. Overprocurement occurred in many regions where food stores ran out, and large numbers of people subsequently died of starvation (Meng & Qian, 2009). As a result, mortality dramatically increased and fertility rates dropped sharply during 1959–1961. The famine led to an estimated 30 million excess deaths and another 30 million lost births (Ashton et al., 1984; Chen & Zhou, 2007; Peng, 1987).

The famine affected rural areas disproportionately (Chen & Zhou, 2007; Huang, Li, Wang, & Martorell, 2010). Urban residents were less impacted by the famine because of preferential treatment by governments through a grain ration system even though rations were cut modestly during the famine years in some regions (Chen & Zhou, 2007). Dramatic regional variations in famine intensity also occurred, evident in the substantial difference in mortality rates across regions in the year 1960. The highest rates were recorded in Anhui (68.6 per thousand) and Sichuan (54.0 per thousand); the lowest rates were in provinces in Northeast China (Liaoning, Heilongjiang, and Jilin, about 11 per thousand). The variation in famine severity was more likely to be determined by the degree of willingness of local leaders to follow the radical central government policies, not local grain production. In fact, high productivity areas were more likely to experience severe famine (Meng, Qian, & Yared, 2010).

Although famines are normally accompanied by migration away from famine areas, the Chinese famine led only to mild mobility, primarily caused by the restriction imposed by the residence registration (*hukou*) system (Chen & Zhou, 2007; Meng & Qian, 2009). *Hukou* regulation was initiated in 1951, formalized, and then strictly reinforced in both cities and rural areas by 1958 (Chan & Zhang, 1999). Under the *hukou* regulation, every citizen was required to register one and only one permanent residency. Regulation on migration was firmly controlled by a public security system, which monitored and controlled not only the rural influx to the cities but also all intrarural and intraurban movement (Chan & Zhang, 1999).

Sex-specific famine effect and natural selection

Recent studies have shown that early-life exposure to the Chinese famine was associated with stunted growth (Chen & Zhou, 2007; Gorgens, Meng, & Vaithianathan, 2012; Huang et al., 2010; Meng & Qian, 2009) and higher risk of adult schizophrenia (St. Clair