Social Science & Medicine 68 (2009) 1315–1321

Contents lists available at ScienceDirect

Social Science & Medicine

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

Famine, death, and madness: Schizophrenia in early adulthood after prenatal exposure to the Chinese Great Leap Forward Famine☆

Shige Song [a,*], Wei Wang [b], Peifeng Hu [c]

[a] Institute of Sociology, Chinese Academy of Social Sciences, Beijing, China
[b] School of Public Health and Family Medicine, Capital Medical University, Beijing, China
[c] UCLA School of Medicine, Los Angeles, USA

ARTICLE INFO

Article history:
Available online 14 February 2009

Keywords:
China
Famine
Differential mortality
Long-term survivor
Survival analysis
Schizophrenia
Selection effect
Lifecourse

ABSTRACT

Using data from large scale, nationally representative sample surveys, we tested the hypothesis that prenatal exposure to famine increases schizophrenia risk at adulthood by studying the Great Leap Forward Famine in China (1959–1961). Our results show that, in the urban population, being conceived and born during the famine increased the risk of developing schizophrenia at early adulthood as compared to both the pre-famine and post-famine cohorts. In the rural population, however, the post-famine cohort had the highest risk of developing schizophrenia, and there was virtually no difference in schizophrenia risk between the pre-famine and the famine cohort. This finding contrasts sharply with previous studies on the Dutch Hunger Winter as well as with smaller scale local studies in China based on hospital records. We offer an explanation for the urban–rural difference in the schizophrenia–famine relationship based on population selection by differential excess mortality and provide supportive evidence through province- and cohort-level ecological analysis

Introduction

Schizophrenia is a multifactorial mental disorder that may be caused by an interaction between adverse genetic and environmental factors beginning in very early stages of the neurodevelopmental process (McGrath, Feron, Burne, Mackay-Sim, & Eyles, 2003; Marenco & Weinberger, 2000; Murray & Lewis, 1987). Many potential environmental risk factors, including prenatal influenza exposure, obstetric complications, season of birth, and prenatal malnutrition, have been suggested, but none have been firmly established (Cannon, 2002; Hultman, Sparen, Takei, Murray, & Cnattingius, 1999; Mortensen et al., 1999; O'Callaghan, Sham, Takei, Glover, & Murray, 1991). The effect of prenatal malnutrition on the subsequent risk of schizophrenia is of particular interest. According to the neurodevelopmental hypothesis, prenatal exposure to malnutrition may increase the risk of schizophrenia at adulthood by disrupting the orderly cascade of fetal brain development, especially in those with a genetic predisposition (Murray & Lewis, 1987; Susser & Lin, 1992; Weinberger, 1987).

Studying the relationship between prenatal malnutrition and schizophrenia has been challenging because virtually no schizophrenia cases occur before the age of 16. The long interval between a prenatal malnutrition insult and the onset of schizophrenia, together with the relatively low prevalence of schizophrenia in the general population, makes it cost-prohibitive to study the direct connection between prenatal malnutrition and adult schizophrenia with adequate controls and reasonable statistical power. The study of the long-term consequences of famine provides a way around this problem. In a sense, famine works like a natural experiment: it creates a cohort of severely malnourished children who differ from children born immediately before and after. As long as each individual's famine exposure status (pre-famine, famine, or post-famine) can be identified, and assuming that people who were conceived or born during the famine had an elevated risk of suffering from prenatal malnutrition, it is straightforward to assess the impact of prenatal malnutrition on selected health outcomes, including schizophrenia, through cohort comparisons.

The main supportive evidence for the hypothesis that prenatal malnutrition increases the risk of schizophrenia later in life comes from studies of the 1944–1945 Dutch Hunger Winter. The Dutch Hunger Winter was caused by a combination of factors, including the Nazi food embargo and an unusually long and harsh winter. These circumstances resulted in approximately 10,000 deaths directly from extreme malnutrition and starvation (Stein, 1975).

☆ The authors would like to thank Drs. Donald J. Treiman and Sarah A. Burgard for helpful comments.

* Corresponding author. Institute of Sociology, Chinese Academy of Social Sciences, 5 Jiannei Dajie, Beijing 100732, China. Tel.: +86 10 64460722.
E-mail address: sgsong@ccpr.ucla.edu (S. Song).

0277-9536/$ – see front matter © 2009 Elsevier Ltd. All rights reserved.
doi:10.1016/j.socscimed.2009.01.027

People conceived or born during the height of the Hunger Winter were twice as likely to develop schizophrenia as those born before or afterwards (Neugebauer, Hoek, & Susser, 1999; Susser & Lin, 1992; Susser et al., 1996).

The Great Leap Forward Famine took place in China in 1959–1961. This famine was caused by natural disaster together with policy mistakes, especially those made during the Great Leap Forward in 1958 (Kung & Lin, 2003). Compared to the Dutch Hunger Winter, the Great Leap Forward Famine lasted much longer (three years versus one year), impacted a much broader geographic area (all of China versus some parts of the Netherlands), and caused much greater mortality (over 30 million deaths in China with a mortality rate of over 3.0%, versus ten thousand deaths in the Netherlands with a mortality rate of about 1.5%) (Ashton, Hill, Piazza, & Zeitz, 1984; Kung & Lin, 2003; Lumey & Van Poppel, 1994). It provides an ideal setting for testing the prenatal malnutrition hypothesis, either to provide further supportive evidence in a drastically different context or to find alternative explanations that have been overlooked in past research. A local study combining hospital records and historical population data has demonstrated a positive link between prenatal exposure to the Great Leap Forward Famine and an increased number of hospitalized adult schizophrenia patients in a Chinese county (St Clair et al., 2005). This study is the first to shed light on this difficult topic, but it suffers from some serious weaknesses. First of all, not all Chinese schizophrenia patients go to a hospital, and the process of deciding who is admitted to a hospital or who receives psychiatric treatment is highly selective. Relying on hospital records thus leads to conclusions based on a biased sample that overrepresents urban patients with relatively higher socioeconomic status (Phillips, 2001). Second, this study failed to control for urban–rural differences, the most important dimension of the social stratification system of Chinese society since the 1950s (Wu & Treiman, 2004). If the cohort pattern of schizophrenia risk differs between urban and rural populations, then results based on hospital patient records, which are predominantly urban, most likely misrepresent the true cohort pattern of the general population in China, which is predominantly rural. Last but not least, results from one local study cannot be generalized to make inferences about the effect of prenatal exposure to the Great Leap Forward Famine on the risk of schizophrenia at the national level.

We address these issues by utilizing a large scale, nationally representative sample survey to compare cohort differences in schizophrenia risk as diagnosed by professional psychiatrists, while controlling for gender and urban–rural differences. Although the urban–rural residence information used in this analysis was pertinent to the time of the survey, it can be used as a good proxy measure of the urban–rural residence when respondents were born for two reasons. First, the level of rural–urban migration was kept at a low level between the late 1950s and early 1980s by a strict internal passport system called the "household registration system" (Wu & Treiman, 2004). Second, there is no reason to expect the rural–urban migration pattern to differ between those who were born before, during, and after the famine, because the strict migration restrictions did not vary by age. Our results represent a significant step forward toward the goal of establishing a causal relationship between prenatal malnutrition and development of schizophrenia during adulthood.

Methods

Data sources

The 1987 Chinese National Disability Sample Survey (CNDSS) is the largest sample survey in the world with a special focus on disability. It used a nationally representative, stratified, multi-stage, clustered sampling design to recruit 369,448 family households and 1,579,316 residents from all 29 provincial level administrative units in China. The interview teams were composed of well-trained professional interviewers and certified medical doctors and were headed by local officials. The interviews were carried out in two steps: a household interview of everyone in selected households to screen for individuals with disabilities, followed by a questionnaire interview with those who were identified as having a disability (National Disability Sample Survey, 1989). CNDSS is the major data source for this research.

A second data source is the 1988 National Survey of Fertility and Contraception in China (NSFCC), also known as the two-per-thousand fertility survey (Lavely, 1991). It is a large scale, nationally representative sample survey with a total of 2.1 million respondents. It records selected women's complete pregnancy histories, from which we computed province- and cohort-specific infant mortality rates and merged into the disability data for the purpose of an auxiliary ecological analysis that strengthens the main findings.

Screening and diagnosis

Screening of individuals with a mental disability (including schizophrenia) in CNDSS relied on a combination of self-report (or family members' report), a short interview (eight questions), and on-site diagnosis by professional psychiatrists. Diagnosis was based on the Chinese Classification of Mental Disorder (CCMD), which shares similarities with the widely used Diagnostic and Statistical Manual of Mental Disorders (DSM) and ICD system, though it includes unique elements (National Disability Sample Survey, 1989). Despite the differences, CCMD yields highly compatible diagnoses to those based on DSM and ICD criteria (Phillips, 2001). Of the 1,579,316 respondents, 3907 were identified as having a mental disorder, and 2574 were identified as having schizophrenia. To minimize confounding with other social changes, we contrasted the famine cohort with both the immediately preceding and immediately following cohorts by restricting our analysis to the 294,365 individuals born between 1955 and 1965. This restriction reduced the number of schizophrenia cases to 494.

Identifying exposure

Significant regional variations exist with regard to onset (1958–1960), duration (2–5 years), and severity of the Great Leap Forward Famine (excess crude death rates ranged from 2.70 to 109.78 per thousand); the severity is largely a function of the famine duration (Kung & Lin, 2003; Peng, 1987). However, the small number of schizophrenia cases in the sample makes more fine-grained statistical analysis difficult. We used province-specific beginning and ending years to define the Great Leap Forward Famine cohorts (Kung & Lin, 2003). Of 29 provinces, the famine started in 1959 and ended in 1962 in 13 provinces. The starting and ending dates of the famine for the remaining 16 provinces are shown in Table 1. Of all 320,503 respondents born in 1955–1965, pre-famine respondents constituted 35% of all cases, post-famine respondents constituted 37% of all cases, and the famine cohort constituted 28% of all cases.

Statistical analysis

Ordinary logistic regression yields biased estimates in the presence of right censoring, as in the current case. At the time of the survey interview in 1987, individuals in the selected cohorts were aged 22–32, the age range during which most schizophrenia cases develop (Stefan, Travis, & Murray, 2002). We have information on