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Research Letter

Urban birth and psychotic experiences in the United States

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Introduction

There is a preponderance of evidence, much of it from Northern Europe, suggesting a link between urban residence and risk for psychotic disorders (1). Since the meanings and correlates of urban living differ across contexts, this association may not be universal (2). In a recent multisite study, the association was evident in Northern Europe, but not in other high-income European countries (e.g., Spain, Italy) (3). Psychotic experiences (PEs) are subclinical manifestations of psychosis (typically mild and transient) that occur in the general population and have been associated with increased risk for common mental disorders and substance use, as well as for psychotic disorders, which are less common. Regarding PEs, one recent study in the United Kingdom supported a relationship with urban birth (4), while another found no such relationship across low- and middle-income countries (5). Although research on the urban environment and psychotic disorders originated partly in the United States (6), there have been few recent studies of this relationship. To our knowledge, this is the first study to examine the relationship between urban birth and PEs in the general U.S. population.

Method

Sample

Participants (N = 2554) were drawn from RAND's American Life Panel, a probability-sampled Internet-based panel study representative of U.S. adults over the age of 17 (https://alpdata.rand.org/). A total of 3932 members were invited to participate in web surveys, and 2555 completed the surveys (completion rate: 64.9%). Respondents were compensated $3. Panelists were provided computer equipment and Internet access if needed. Data were collected February–April, 2019.

Measures

PEs were measured using the four-item WHO psychosis screen; respondents endorsing any of the experiences were coded as having lifetime PE and were then asked whether these experiences occurred in the past 12 months. Urban birth was measured using a single item: "Describe the area in which you were born." Respondents could answer large urban (>500 000 people), small urban (<500 000 people), suburban, or rural. Sociodemographic covariates included sex (male, female), age (continuous), and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic/Latino, Other).

Analysis

Multivariable logistic regression models estimated the association between urban birth and lifetime and 12-month PE adjusted for demographic covariates. Sensitivity analyses investigated associations (i) using alternate binary codings of urban birth and (ii) stratifying by sex, race (White vs. non-White), and age (18–40 vs. 41-100). All data were weighted to represent U.S. households. Results are presented as odds ratios (ORs) with 95% confidence intervals (CI). Statistical significance was set at the conventional level of two-tailed a = 0.05.

Results

About 17.54% (SE 0.90) and 8.89% (SE = 0.68) of the weighted sample reported having lifetime and 12-month PE respectively. About 31.96% (SE = 1.04) of the sample was born in large urban areas, 27.73% (SE = 0.90) in small urban areas, 18.25% (SE = 0.87) in suburban areas, and 22.05% (SE = 0.93) in rural areas. The average

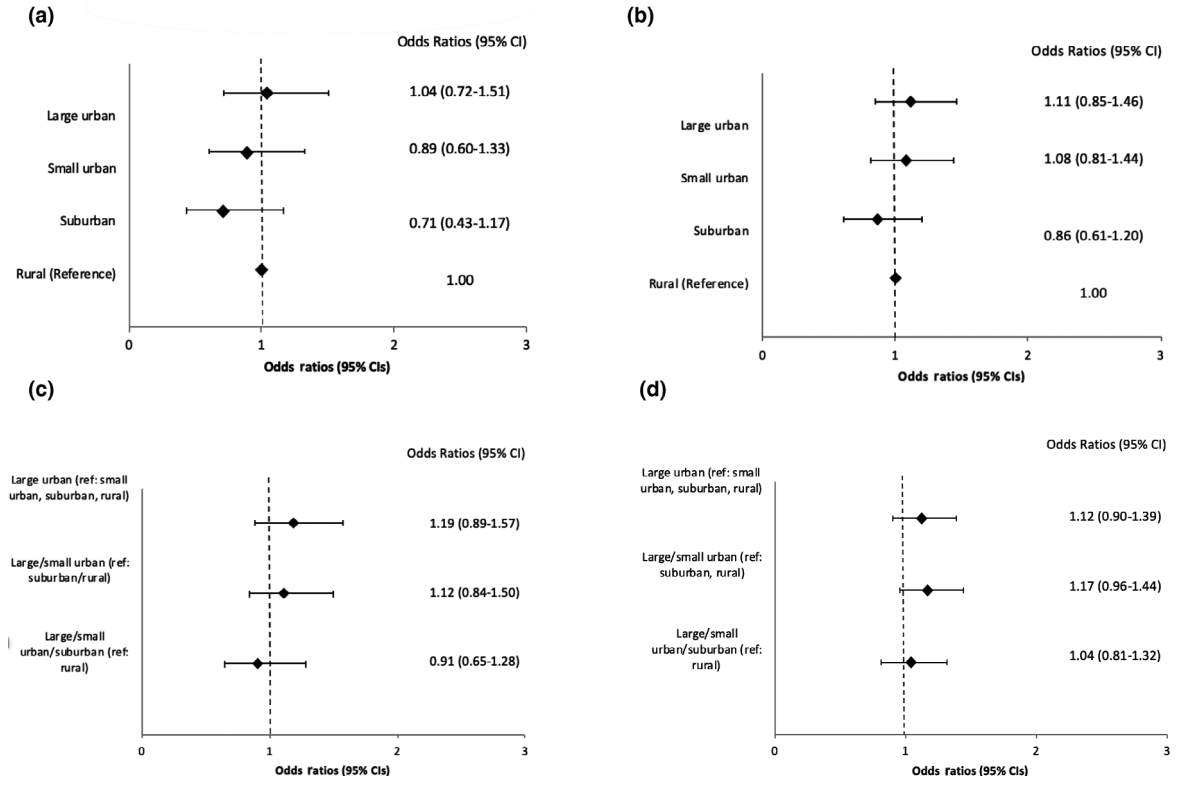

Fig. 1. (a) Associations between urban birth and 12-month psychotic experiences. (b) Associations between urban birth and lifetime psychotic experiences. (c) Sensitivity analyses examining associations between urban birth and 12-month psychotic experiences using various binary codings of the exposure. (d) Sensitivity analyses examining associations between urban birth and lifetime psychotic experiences using various binary codings of the exposure.

age of the sample was 57 years, and the sample was 56.87% women and 43.13% men. The sample was predominantly White (70.76%, SE = 2.04). In multivariable models, urbanicity was not significantly associated with 12-month (Fig. 1a) or lifetime (Fig. 1b) PEs after adjusting for age, sex, and race. Sensitivity analyses showed that urban birth was not significantly associated with PEs even when coding the exposure variable differently (Fig. 1c,d), or when stratifying by age, sex, or race (results available upon request).

Discussion

In a U.S. general population sample, we found no evidence of a relationship between urban birth and 12-month or lifetime PE. Our findings should be interpreted bearing in mind potential limitations. First, the data were cross-sectional, limiting causal inference. Thus, future research should examine urban living and incidence of PEs over time, as associations may vary across the life course. Second, the response rate was 64.9%, which is typical for online panel surveys, but still susceptible to non-response bias. Third, the self-report urban birth item was not an externally validated measure, although similar items have been used in prior studies. Finally, depending on how urbanicity was coded, the point estimates loosely indicated urban birth was associated with a slightly elevated risk for PEs, but lacked statistical significance at the conventional level, raising the possibility that our analyses were inadequately powered to detect effect sizes of this magnitude. Thus, we cannot conclusively confirm the null hypothesis that urban birth is not associated with PEs, which should be further investigated in future studies using larger samples and incidence data. Such studies should specifically examine whether (and why) urbanicity may be differentially associated with psychosis (both disorders and experiences) across and within countries, which may help elucidate the etiology of psychosis.

Conflict of interest

None.

Data availability statement

Data are available at https://www.rand.org/research/data/alp.html

Hans Y. Oh[1], *Ezra Susser*[2], *Ai Koyanagi*[3,4], *Ian Kelleher*[5], *Jordan E. DeVylder*[6]
[1]*Suzanne Dworak-Peck School of Social Work, University of Southern California, Los Angeles, CA,* [2]*Mailman School of Public Health, Columbia University, New York, NY, USA,* [3]*Research and Development Unit, Parc Sanitari Sant Joan de Déu, CIBERSAM, Barcelona,* [4]*ICREA, Barcelona, Spain,* [5]*Department of Psychiatry, Royal College of Surgeons in Ireland, Dublin, Ireland and* [6]*Graduate School of Social Service, Fordham University, New York, NY, USA*
E-mail: hansoh@usc.edu

REFERENCES

1. March D, Hatch SL, Morgan C, et al. Psychosis and place. Epidemiol Rev 2008;**30**:84–100.
2. Kirkbride JB, Keyes KM, Susser E. City living and psychotic disorders—implications of global heterogeneity for theory development. JAMA Psychiatry 2018;**75**:1211–1212.
3. Jongsma HE, Gayer-Anderson C, Lasalvia A, et al. Network of National Schizophrenia Networks Studying Gene-Environment Interactions Work Package 2 (EU-GEI WP2) Group. Treated incidence of psychotic disorders in the multinational EU-GEI study. JAMA Psychiatry 2018; **75**:36–46.
4. Solmi F, Lewis G, Zammit S, Kirkbride JB. Neighborhood characteristics at birth and positive and negative psychotic symptoms in adolescence: findings from the ALSPAC Birth Cohort. Schizophr Bull 2019. https://doi.org/10.1093/schbul/sbz049
5. DeVylder JE, Kelleher I, Lalane M, Oh H, Link BG, Koyanagi A. Association of urbanicity with psychosis in low- and middle-income countries. JAMA Psychiatry 2018;**75**:678–686.
6. Faris REL, Dunham HW. Mental disorders in urban areas: an ecological study of schizophrenia and other psychoses. 1939. Oxford, England: Univ. Chicago Press.

The HLA 8.1 ancestral haplotype in schizophrenia: dual implication in neuro-synaptic pruning and autoimmunity?

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Schizophrenia (SZ), a neurodevelopmental disorder, is one of the most severe and common psychiatric conditions, affecting globally 1% of adult population. Stemming from complex gene-environment interactions, in a significant subset of patients, SZ is characterized by immune dysfunctions that include early inefficient anti-infectious responses as well disease-associated chronic low-grade inflammation and comorbid autoimmune conditions (1). In such intersections between infection, inflammation and autoimmunity, the key genetic platform for both innate and adaptive immune processes is the major histocompatibility complex (MHC) which encompasses the prominent human leukocyte antigen (HLA) region. The HLA system is the most polymorphic region of the human genome, and its allelic diversity is essential for antigen presentation to immune effector cells and downstream humoral and cellular immune responses. Hence, characterizing the HLA allelic diversity allows not only to evaluate the potential genetic relationship between the HLA system and a given disease but also to understand its impact on pathophysiological processes (2).

Recent genome wide association studies (GWAS), especially the one involving more than 36989 patients SZ patients and 113075 healthy controls, showed that the most significant genome wide association signal lies in the HLA-hosting MHC region, thus further highlighting the importance of immunogenetic processes in conferring SZ risk (3). Nevertheless, the fine details of the underlying mechanisms remain elusive but the dual implication of the HLA system both in neurodevelopment and inflammatory/autoimmune diseases is of interest in the psychiatric context. In the era of global genomics, assignment of classical HLA alleles requires specifically designed imputation methods. When applied in some of the above-mentioned GWAS, they uncovered not only risk alleles but also some protective variants, the latter ones strikingly derived from the so-called 8.1 "autoimmune" ancestral haplotype (8.1 AH) (A*01 ~ B*08 ~ DRB1*03 ~ DQB1*02) (4). Of interest, the 8.1 AH is known to be positively associated with risk for (auto) immune disorders and is characterized by elevated circulating levels of proinflammatory cytokine, namely tumor necrosis factor alpha (TNF-α) in healthy individuals. The latter may explain the reported association of 8.1 AH with protection against infectious events (5). By conferring susceptibility to autoimmune disorders on one hand and protection against infections on the other, the 8.1 AH can be considered as a prototypic example of evolutionary-genetic trade-offs in conferring diametric disease risks further influenced by genetic and