

Mind and the city: The association between urban living and schizophrenia

Yuning Jackie Tang

University of Toronto

In the past sixty years, our social landscape has changed at an unprecedented pace. Prompted by the rapid growth of industry, improved transportation, and alterations in economic structure, we have transitioned from a rural-centred to urban-centred society. In 1950, less than one third of the world lived in cities, whereas today, over half of the population reside in urban areas, and by 2050, this number is projected to reach 70%.¹ Although urban dwellers are usually wealthier and have better nutrition and easier access to health care services compared to their rural counterparts, the effect of urban living on mental health appears to be largely negative.³ Specifically, the urban environment may be a crucial stimulus in promoting schizophrenia, a debilitating neuropsychiatric disorder characterized by chronic or recurrent psychosis.²

Epidemiological studies beginning in the 1990s, and their subsequent meta-analysis, uniformly suggest that the incidence of schizophrenia in urban areas is two-to three-fold higher than rural areas.³⁻⁵ These studies address a wide range of possible confounders such as age, sex, ethnicity, drug use, social class, and family history, but none of these are able to explain this striking association.³ More importantly, one third of all such research reveals a “dose-response” relationship between the number of years lived in urban areas and an increased risk of schizophrenia.⁶ Naturally, an important question that emerges from these epidemiological studies is whether the association between urbanicity and schizophrenia is correlative or causal. For example, an alternative explanation is that urban dwelling is not causing the increased prevalence of schizophrenia, but instead, individuals genetically at risk of the disease tend to reside in urban areas. Although not yet definitive, current evidence suggests this hypothesis is unlikely to account for the major part of the association.³ First, studies that adjusted for genetic predisposition of schizophrenia only found slightly reduced associations with urbanicity.³

Furthermore, early exposure to urban environment during upbringing is associated with a higher risk of schizophrenia in adulthood, even after the individual is removed from urban centres.^{7,8} Taken together, these results suggest that not only the association between urbanicity and schizophrenia is likely true, but urbanicity may actually have a causal role in the etiology of this disease.

To date, the mechanism that underlies the link between urbanicity and schizophrenia remains a mystery. This is largely attributed to the enormous complexity of the urban environment and our limited knowledge in the neurobiology of the disease itself. Nonetheless, the burgeoning field of social neuroscience is beginning to shed some insights into this issue. In a pioneering work from Germany, researchers used functional magnetic resonance imaging to compare the brain's stress response between 55 urban and rural residents. The amygdala, a part of the brain that processes negative emotion, and the perigenual anterior cingulate cortex (pACC), which regulates the amygdala shows particularly interesting results.⁷ Activation of the amygdala is positively correlated with the participants' city size, and activation of pACC correlated with the duration of the city habitation.⁷ Importantly, the synaptic connectivity between amygdala and the pACC is diminished in individuals from urban areas compared to rural areas, indicating a potential of reduced inhibition of the amygdala.⁷ Therefore, the increased incidence of schizophrenia among city dwellers may be caused by an overly-active stress response in the brain. Consistent with this, individuals that encountered stressful experiences, such as childhood trauma or social defeats had an increased risk for developing schizophrenia.⁹ It is conceivable that the relentlessly stressful city environment, with insults such as overcrowding, high crime rates, heavier pollution and noise, over time, can cause in aberrant alterations in the stress signaling pathway, contributing to the increased incidence of schizophrenia.¹⁰ ▶

As we continue to move forward in the age of global urbanization, the task of understanding the link between city environment and mental health is increasingly urgent. Megacities in developing countries such as China, India and Brazil are growing at lightning speed and the cost of care for mental health is rising. Pinpointing the factors in urban environments that contribute to schizophrenia may allow policy makers and healthcare professionals to implement effective interventions to prevent and combat this illness. In fact, some of our most successful attempts in reducing the global disease burden came from reducing exposure to environmental risk factors. For instance, anti-smoking campaigns reduced the incidence of lung cancer and improved sanitation has led to a worldwide decline of infectious diseases.⁵ Currently, the major challenge to improve mental illness prevention with environmental measures is the lack of efficient translational strategies that can bridge basic research to the clinical and population level. Greater multidisciplinary collaboration between diverse fields such as psychiatry, neuroscience, genetics, and social sciences is necessary to delineate and curtail the effect of urbanicity on schizophrenia. ■

References

1. Fund UNP. State of World Population 2007: Unleashing the Potential of Urban Growth. Population and Development Review. 2007;33(3).
2. Ross CA, Margolis RL, Reading SA, Pletnikov M, Coyle JT. Neurobiology of schizophrenia. *Neuron*. 2006 Oct 5;52(1):139-53. PubMed PMID: 17015232.
3. Krabbendam L, van Os J. Schizophrenia and urbanicity: a major environmental influence—conditional on genetic risk. *Schizophrenia bulletin*. 2005 Oct;31(4):795-9. PubMed PMID: 16150958.
4. Vassos E, Pedersen CB, Murray RM, Collier DA, Lewis CM. Meta-analysis of the association of urbanicity with schizophrenia. *Schizophrenia bulletin*. 2012 Nov;38(6):1118-23. PubMed PMID: 23015685. Pubmed Central PMCID: 3494055.
5. Brown AS. The environment and susceptibility to schizophrenia. *Progress in neurobiology*. 2011 Jan;93(1):23-58. PubMed PMID: 20955757. Pubmed Central PMCID: 3521525.
6. Pedersen CB, Mortensen PB. Evidence of a dose-response relationship between urbanicity during upbringing and schizophrenia risk. *Archives of general psychiatry*. 2001 Nov;58(11):1039-46. PubMed PMID: 11695950.
7. Lederbogen F, Kirsch P, Haddad L, Streit F, Tost H, Schuch P, et al. City living and urban upbringing affect neural social stress processing in humans. *Nature*. 2011 Jun 23;474(7352):498-501. PubMed PMID: 21697947.
8. Meyer-Lindenberg A, Tost H. Neural mechanisms of social risk for psychiatric disorders. *Nature neuroscience*. 2012 May;15(5):663-8. PubMed PMID: 22504349.
9. Selten JP, Cantor-Graae E. Social defeat: risk factor for schizophrenia? *The British journal of psychiatry : the journal of mental science*. 2005 Aug;187:101-2. PubMed PMID: 16055818.
10. Arnsten AF. Stress signalling pathways that impair prefrontal cortex structure and function. *Nature reviews Neuroscience*. 2009 Jun;10(6):410-22. PubMed PMID: 19455173. Pubmed Central PMCID: 2907136.

Yuning Jackie Tang

Yuning Tang is a Masters student in the Department of Laboratory Medicine and Pathobiology at the University of Toronto. His research focuses on using next-generation sequencing to study the genetic mechanisms that contribute to the sarcoma development.