



Letter to the editor

Ecosystem approaches to the risk for schizophrenia



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To the Editor:

Engemann et al. (2019) recently showed that growing up in natural, non-urban surroundings may decrease rates of schizophrenia through multiple pathways. In fact, evidence is building towards a matrix of social and environmental factors operating across generations in the pathogenesis of schizophrenia (Stilo and Murray, 2019). In this context, we argue that ecosystem approaches to health are needed to achieve a comprehensive model of the environmental risk for schizophrenia, with the overarching goal of tackling its underlying health inequities.

Many environmental factors from pre-conception to adulthood have been found to predict the risk for schizophrenia. These include early-life ecological exposures such as natural disasters, air pollution and heavy metals (Engemann et al., 2019; King et al., 2010; Stilo and Murray, 2019). Interspecies relationships, in the form of prenatal or childhood exposure to *Toxoplasma gondii* and other infectious agents, constitute another class of risk factors (King et al., 2010; Stilo and Murray, 2019). Social and geopolitical risk factors for schizophrenia have also emerged across several populations, including social isolation, parental socio-economic status, bigenerational migration status and war (King et al., 2010; Stilo and Murray, 2019).

Studying the single contributions of specific environmental exposures in the pathogenesis of schizophrenia is challenging, as these factors are dynamically interconnected and interdependent over time. Prenatal maternal stress, for example, may increase the risk for schizophrenia in offspring through maternal subjective distress, obstetrical complications, health-impairing behaviors, or other pathways (King et al., 2010; Lipner et al., 2019). These pathways converge downstream to biological mechanisms such as maternal immune activation (Lipner et al., 2019). Further, prenatal maternal stress, such as daily life hassles, may also be a proxy variable for inheritable or familial vulnerability factors (King et al., 2010). Environmental risk factors appear to individually contribute small increases in the absolute risk for schizophrenia, while multiple interactions between environmental and genetic variables probably explain a much larger proportion of the variance in risk (King et al., 2010; Stilo and Murray, 2019).

Hence, conceptualizing socio-environmental exposures as jointly operating in a system – the ecosystem – is a step towards a more comprehensive model of the risk for schizophrenia. The ecosystem is a unit encompassing ecological, socio-cultural and biological layers of health

determinants (Webb et al., 2010). Alterations in any of these interdependent spheres can impact human health through a variety of pathways, and human actions can reciprocally transform the ecosystem.

In epidemiological research, the intricacy of ecosystem factors participating in the pathogenesis of schizophrenia translates into many potential interacting and confounding variables. Prospective, longitudinal studies of population-wide ecosystem alterations can disentangle the complex environmental factors at play. For example, prenatal maternal exposure to disasters or pandemics occurs quasi-randomly and produces rapid ecosystem changes (King et al., 2010). The COVID-19 pandemic illustrates the relevance of this approach, as maternal social distancing and health risks during pregnancy can have multiple effects (known or speculative) on the early pathogenesis of schizophrenia (see Fig. 1). Research on prenatal exposure to the pandemic may consider how prenatal stress and maternal immune activation are affected by, among others; (1) the risks of maternal coronavirus infection, (2) the effect of social distancing on stress and its interaction with partner support (Brock et al., 2014), (3) the effect of social distancing on access to perinatal care (Kildea et al., 2018), and (4) the effects of urbanicity, notably in a context of potential decrease in air pollution and traffic noise (Cai et al., 2017).

Ecosystem approaches to health draw from various bodies of knowledge to achieve critical systems understanding and problem solving (Webb et al., 2010). Increasingly, they aim to engage with and empower communities in guiding research directions and policy decision-making. The recent case of an ecosystem approach to the health of the Inuit population of Nunavik (Northern Quebec, Canada) embodies these objectives and illustrates the model's relevance in translational research. Blood methylmercury levels have been found to be high in a large percentage of the population of Nunavik, and were traced back to the consumption of some marine mammals contaminated by global ocean pollution. To promote the multiple benefits of wild marine foods while preventing the adverse effects of prenatal exposure to methylmercury on child development, scientists, community stakeholders and the regional public health board joined forces to develop and implement prevention strategies for childbearing-age women (Lemire et al., 2015; Pirkle et al., 2016). Thereby, the integration of disciplines over time, from marine biology to nutrition to neurodevelopment, together with collaboration across sectors, allowed an ecosystem approach to hopefully better foster healthy pregnancies and child development in Nunavik.

In summary, we argue that the dynamic, interdependent socio-environmental underpinnings of the risk for schizophrenia warrant an ecosystem approach. This approach serves as a framework for comprehensive studies that integrate multiple individual and environmental factors, in tandem with interdisciplinary and intersectorial efforts towards clinical and public health translations of findings.

Declaration of competing interest

The authors declare that there is no conflict of interest regarding the publication of this article.

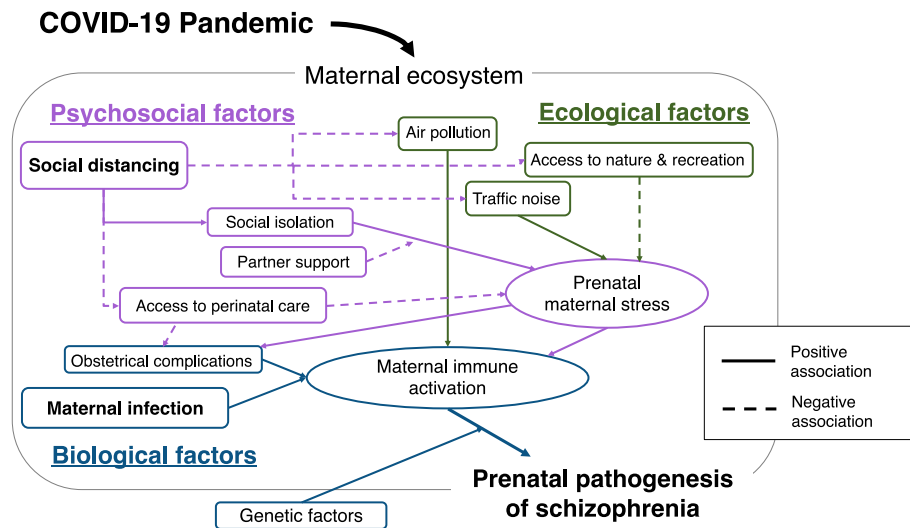


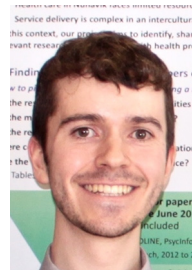
Fig. 1. Prenatal maternal ecosystem in the context of the COVID-19 pandemic (within urban settings). Non-exhaustive, proposed pathways start from (1) social distancing and (2) the risk of maternal infection as primary consequences of the pandemic, and unfold into a network of ecological, psychosocial and biological factors influencing the early pathogenesis of schizophrenia in offspring through maternal immune responses.

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