

The Contribution of Social Factors to the Development of Schizophrenia: A Review of Recent Findings

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Objective: To investigate recent evidence suggesting that social factors are causally related to the development of schizophrenia.

Method: I conducted a systematic review of MEDLINE to identify possibly relevant studies. The search was limited to peer-reviewed studies and review articles appearing in English-language journals since 1996. Studies were included if they used standardized diagnostic criteria for schizophrenia or standardized assessment instruments for psychotic symptoms.

Results: Studies of migrants to western Europe provide compelling support for the notion that social factors contribute to the development of schizophrenia. Findings such as excessively high risk for schizophrenia in second-generation immigrants are difficult to explain solely in terms of biological or genetic factors. A growing number of studies implicate childhood exposure to social adversity as a risk factor for schizophrenia, although few studies have used prospective designs. The increased incidence of schizophrenia risk associated with urban birth and (or) urban upbringing suggests possible social causation, but these findings are more ambiguous. Thus far, no studies have explored actual mechanisms by which exposure to social factors might generate psychotic symptoms, although animal experiments suggest that social defeat or social exclusion may cause dopamine dysregulation or sensitization.

Conclusions: The accumulating evidence suggesting a role for social factors in the development of schizophrenia arises primarily from studies of migrants conducted in Europe. The mechanisms by which social factors exert their influence remain unknown. Future investigations of social causation should clarify the temporal relation between exposure to social defeat and (or) social adversity and the development of psychotic symptoms.

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Clinical Implications

- Social factors may play an etiologic role in the development of schizophrenia.
- A common denominator may be chronic experiences of social defeat and (or) exclusion, resulting in dopamine dysregulation or sensitization.
- The implementation of interventions and preventive strategies may reduce the risk associated with social factors.

Limitations

- Thus far, few prospective studies specifically target social factors.
- Animal models of social defeat may not be satisfactory analogues for the migrant experience.
- The role of substance abuse in individuals exposed to social adversity cannot be excluded.

Key Words: *schizophrenia, social factors, migrants, urbanization, etiology*

Schizophrenia is generally regarded as a disorder with genetic determinants¹ and neurodevelopmental antecedents,² although the exact causes are still unknown. Current research activity is largely concerned with the search for the neurobiological substrates of the disorder and the identification of the leading candidate gene(s). However, concordance rates in monozygotic twins that range between 40% and 60%¹ suggest that aspects of the environment may play a causal role in the development of schizophrenia. Despite this widely known finding, the notion that social factors may contribute to schizophrenia remains controversial.³ In Europe, during the past decade, the plausibility of the social causation hypothesis has increasingly gained momentum,³⁻⁵ primarily owing to studies of urbanization and migration.⁶⁻⁷

Although the emergence of a biopsychosocial point of view in schizophrenia research is a recent development, ethnic and urban-rural variations in the distribution of schizophrenia were observed in the United States as early as the first half of the 20th century. Using data on first admissions to Rochester Hospital in Minnesota, Ødegaard⁸ found a twofold increase in admission rates for schizophrenia among Norwegian immigrants, compared with individuals born in the United States and Norwegians living in Norway. Ødegaard attributed his findings among immigrants to negative selection, that is, to schizoid features predisposing individuals to migration.

Malzberg, another early pioneer, used data from hospital admissions in New York State and population denominators derived from censuses to show that foreign-born migrants had higher rates than nonmigrants for dementia praecox, even after adjustments for age differences.⁹⁻¹¹ Noting that rates for dementia praecox were higher in New York City than in the more rural areas of New York State, Malzberg also adjusted his results for urbanization.¹⁰⁻¹¹ Throughout his lifetime, however, Malzberg remained uncertain about the mechanism underlying these findings, and attributed them variously to selection processes and (or) to social stressors associated with migration. Malzberg was also one of the first to observe that schizophrenia rates varied according to the relative size of an ethnic group in a given neighbourhood. In his studies of native-born internal migrants in Canada,¹² Malzberg found that, when an ethnic group constituted the minority in a given

area, first-admission rates of dementia praecox for that group were higher than those for the majority population. These findings have been replicated by several researchers in various settings^{13,14} and are collectively referred to as the “ethnic density” effect.

In the mid-1960s, with the first reports of elevated rates of schizophrenia among African-Caribbean individuals living in the United Kingdom, the investigative focus on migrants shifted toward Europe.¹⁵ Accumulating evidence from several decades of European research now shows that the migrant effect is not specific for African-Caribbeans but is found across first- and second-generation immigrant groups of widely varying origin.⁷ A recent Danish population-based cohort study showed that all foreign-born individuals (regardless of origin) resident in Denmark prior to their 15th birthday had an increased risk of developing schizophrenia.¹⁶ Moreover, an increased risk for schizophrenia was also found in native-born Danes with a history of foreign residence prior to their 15th birthday,¹⁶ indicating that migration confers an increased risk for schizophrenia that is independent of foreign birth. Findings in migrants that cannot be attributed to selection factors have created a need for alternative explanations to Ödegård’s selection hypothesis.

Parallel to these developments, other researchers have drawn attention to possible limitations of the neurodevelopmental model, and in particular, to the challenge posed by the emergence of schizophrenia in early adulthood.¹⁷ Thus it has become increasingly important to explain the pathway by which neurodevelopmentally compromised individuals develop overt symptoms or cross over the vulnerability threshold to “caseness.”¹⁷ Moreover, a growing number of studies indicate that a proportion of the population may have psychotic experiences without fulfilling diagnostic criteria for psychosis or without seeking treatment,¹⁸⁻²⁰ indicating that the boundaries of the schizophrenia phenotype extend beyond a narrowly defined clinical entity.¹⁸ Further, the fact that the prevalence of hallucinations and odd beliefs varies across ethnic groups²¹⁻²³ suggests increasingly that psychotic experiences may have social or cultural determinants. Thus epidemiologic findings that do not fit easily into the neurodevelopmental model have generated an interest in a social causation model of schizophrenia.

The purpose of this review is to critically examine recent evidence suggesting that social factors contribute to the etiology of schizophrenia and to highlight possible methodological issues and problems that need to be resolved.

Method

I conducted a systematic MEDLINE search to identify studies examining the relation between social factors and the development of schizophrenia. The following search terms were

Abbreviations used in this article

CI	confidence interval
RR	relative risk
SES	socioeconomic status

used: schizophrenia, psychosis, social factors, and social environment, along with various synonyms for these terms, with link-outs from key articles. The search was limited to peer-reviewed studies and review articles appearing in English-language journals from 1996 to 2006. Literature lists were also cross-referenced to identify relevant articles. Studies were considered relevant if patients or populations were examined according to standardized diagnostic criteria for schizophrenia or schizophrenia-like psychoses or with standardized instruments for the assessment of psychotic symptoms.

Evidence From Migrant Studies

A recent metaanalysis provides a systematic summary of migrant studies from 1977 to 2003.⁷ All studies were conducted in Europe, except for one in Australia.²⁴ The strength and consistency of the association between migration and schizophrenia is shown in the total data set, comprising 50 effect sizes for first- and second-generation immigrants. In that data set, the overall RR for developing schizophrenia associated with migration was 2.9 (95%CI, 2.5 to 3.4). This risk is greater than most other risk factors associated with schizophrenia, with the exception of family history of psychosis.² RRs were especially high in second-generation immigrants (RR 4.5; 95%CI, 1.5 to 3.1) and in immigrants from countries where the predominant skin colour is “black” (RR 4.8; 95%CI, 3.7 to 6.2). Notably, studies of the sending countries have found normal incidence rates of schizophrenia.^{25–27} The unusually high risks for second-generation immigrants are striking, insofar as they cannot be attributed to the selective migration of persons who are already ill or in the prodromal phase, nor can they be attributed to genetics.^{28–29} Viable explanations for the migrant effect must meet the challenge posed by the increased rates found in both first- and second-generation immigrants. Very few of the hypotheses concerning migrants that have been set forth thus far would satisfy this requirement.⁷ Thus, for example, impaired immunity to a neurotrophic virus found only in Europe would not explain the increased rates in second-generation immigrants, compared with those of the first generation, and prenatal exposure to vitamin D deficiency would not explain the increased rates in first-generation immigrants, compared with the general population. Indeed, the broad ethnic spectrum implicated in these findings seems to refute the notion that any single biological or genetic factor can provide an adequate explanation. However, significant heterogeneity was found across studies; thus, the different migrant groups cannot be regarded as coming from a single population having a common effect size. Also, with some exceptions, few studies examined all migrant groups in a given country, and specific groups with high risks—such as the Surinamese in The Netherlands—have received more attention.

The authors of the metaanalysis argue that social causation is the most likely unifying hypothesis for findings of increased schizophrenia risk in immigrant groups as disparate as Africans and Greenlanders, and they suggest that the underlying common feature is long-term exposure to social defeat or chronic experiences of discrimination.^{5,7} This interpretation is based partly on the observation that especially high RRs for schizophrenia (that is, $RR > 2.9$) were found in groups having certain characteristics, specifically, “black” skin colour, origin in a developing country, or second-generation immigrant status. The higher rates generally found in second-generation, compared with first-generation, immigrants would be attributable to the particularly devastating effect of being treated as an “outsider” in one’s own birth country.^{5,7} The extent to which the increased risk of schizophrenia found in second-generation immigrants is confounded by other factors associated with an increased risk of schizophrenia—for example, urban birth, urban upbringing, and substance abuse—remains unknown.

The social defeat hypothesis has the advantage of being one of the few social causation models that attempts to integrate psychosocial and biological mechanisms to account for the development of psychotic symptoms. According to this model, chronic and long-term experiences of social defeat lead to sensitization of the mesolimbic dopamine system and (or) to increased baseline activity of this system and, thereby, to an increased risk for schizophrenia.^{5,7} These inferences are based largely on results from animal experiments showing that social dominance has an effect on synaptic dopamine levels.^{30,31} Thus, for example, macaque monkeys exposed to social isolation (individual housing) and social subordination showed dopaminergic hyperactivity and also increased vulnerability to the reinforcing effect of cocaine.³⁰ Moreover, rats exposed to social defeat stress (the defeated intruder paradigm) show elevated levels of dopamine in the nucleus accumbens and prefrontal cortex.³¹ In rats, isolation (that is, individual housing) after a single exposure to social defeat augments stress-induced alterations in the dopaminergic system, whereas a familiar social environment seems to prevent these adverse consequences.³² Further, repeated exposure to social-defeat stress in rats leads to increased self-administration of cocaine and amphetamine and to increased sensitivity to these substances.³³ It may be noted that many schizophrenia patients show an increased sensitivity to the psychotogenic effects of illicit drugs and that dopamine dysregulation appears to be present in patients at illness onset and during periods of relapse.³⁴

Thus far, the social defeat hypothesis has not been tested in experiments involving human subjects, and retrospective reports concerning social defeat may be uninformative owing to recall bias. Nevertheless, a prospective study conducted in

The Netherlands showed that previously healthy individuals who reported experiences of discrimination subsequently developed psychotic symptoms.³⁵ Also, 2 recent studies^{36,37} have corroborated the metaanalysis findings. First, a 3-year incidence study in Sweden found that the highest RRs for developing a psychotic disorder were in first-generation immigrants with “black” skin colour (RR 5.8; 95%CI, 2.8 to 13.4) and with birthplace in a developing country (RR 3.3; 95%CI, 2.3 to 4.8).³⁶ Second, in a recently conducted multi-centre study in the United Kingdom, some of the highest-ever reported incidence rates of schizophrenia were found among the African-Caribbean and black African study groups.³⁷ Although rates for the other ethnic groups were more modest, elevated incidence rates for psychoses were found in all ethnic groups, compared with the white British population.³⁷ Thus far, a major limitation in the migrant literature is that few large-scale studies of second-generation immigrants have been conducted. Indeed, the number of effect sizes for second-generation immigrants included in the metaanalysis was limited ($n = 7$). Also, most of the studies included in the metaanalysis did not control for parental social class. The extent to which the migrant effect is reducible to low parental social class remains an issue. It has been argued that the excess risk found in the African-Caribbean and black African populations in the United Kingdom may partly be due to social disadvantage, that is, to low SES, lower educational achievement, higher rates of unemployment, and poorer housing conditions³⁸; however, explanations emphasizing social class and social adversity would still need to specify the underlying mechanisms by which such factors might lead to a brain disorder such as schizophrenia. In contrast, the social defeat hypothesis attempts to provide a plausible neurobiological pathway.⁵ Accordingly, it may be more appropriate to regard the types of social disadvantage found among immigrants as consequences of institutionalized racism and discrimination rather than as illness determinants. Low SES, poor education, and long periods of unemployment are associated with social exclusion,³⁹ which lends further support to the notion that social defeat may be a common denominator. In this regard, it may be important that no consistent relation between parental social class and schizophrenia has been indicated across studies, although associations with higher⁴⁰ and lower⁴¹ parental social class have been found. Also, some immigrant groups, such as the Turks in The Netherlands, have low levels of employment and low levels of educational achievement but, also, low risks for schizophrenia.⁴² Thus the amount of deprivation relative to one’s expectations and ambitions may be more important than absolute levels of deprivation. Low social class in and of itself is unlikely to entirely account for the increased risk of schizophrenia found in migrants to Europe.

Social Inequality, Social Adversity, and Family Upbringing

A growing number of primarily European studies suggest that social factors at birth or during upbringing may be causally related to schizophrenia. Nevertheless, the presence of clinical or subclinical psychosis in parents may contribute to poor social environment, in addition to increasing the risk for schizophrenia in their offspring. Parental mental illness is thus a potential confounding influence in studies of this type. However, even after adjustment for parental mental illness, Harrison et al⁴¹ found that, in Nottingham, measures of SES at birth were related to the development of schizophrenia in adulthood. Intriguingly, the risk for schizophrenia increased with increasing levels of deprivation at birth, providing compelling evidence for a causal relation. The authors concluded that, whatever the nature of the risk factors involved, environmental factors play a significant role in the etiology of schizophrenia.⁴¹ Indeed, a common problem for studies of social deprivation or social adversity (either at birth or during upbringing) is the delineation of the underlying mechanism. Social deprivation at birth can implicate exposures that are not necessarily social, such as genetic effects and prenatal exposure to infection or toxic agents, as well as psychosocial stressors during upbringing.

Several studies of social adversity have focused on exposure during upbringing, highlighting factors such as household type, housing, and welfare assistance. In a sophisticated multigenerational study of immigrant households, Hjern et al⁴³ examined factors related to social adversity, such as parental unemployment, single-parent household, urban residence, adults receiving social welfare benefits, housing, and parental SES. Using register-based data from a Swedish national cohort, the authors compiled rates of schizophrenia and schizophrenia-like psychoses for an adult first-generation immigrant group and for a youth group (specifically, first- and second-generation immigrants born between 1968 and 1979). When rates for these groups, compared with native Swedes, were adjusted for household indicators of social adversity, social adversity explained a sizable proportion of the elevated rates of schizophrenia in the adult group and, to a lesser extent, in the youth group.⁴³ It should be kept in mind that, in the adult group, social adversity could be caused by illness or social drift. In the youth group, where social drift is unlikely, the pathway by which social adversity leads to schizophrenia still needs to be elucidated.

However, the extent to which the risk for schizophrenia associated with social adversity during upbringing can be explained by substance abuse in adolescence and young adulthood remains uncertain. Two recent reviews of the association between cannabis use and the risk for schizophrenia conclude that cannabis is causally related to

schizophrenia.^{44,45} Although cannabis abuse might explain some of the risk for schizophrenia associated with social adversity, it is unlikely that cannabis abuse can entirely explain the increased risk of schizophrenia found in migrants. The twofold risk associated with cannabis is somewhat smaller than the effect size indicated by migration. Moreover, substance abuse is generally more prevalent among male individuals,⁴⁶ whereas the migrant metaanalysis found no sex differences in schizophrenia risk.⁷ Also, Veen et al⁴⁷ found no difference in actual drug use between Dutch-born and immigrant patients with a first episode of psychosis. However, Hjern et al⁴⁸ found that rates of illicit drug abuse were higher in second-generation immigrants than in native Swedes. The contribution of substance abuse to elevated rates of schizophrenia in migrant populations clearly merits further investigation.

Social adversity during upbringing may mediate its effect through aspects of the physical, rather than social, environment. Most immigrants cluster in areas with low-cost housing, household crowding, and high levels of environmental pollutants such as lead. However, studies conducted in Denmark and Finland found that neither household crowding^{49,50} nor exposure to road traffic (that is, to agents such as benzene, carbon dioxide, lead, or noise)⁵¹ were risks for schizophrenia. Also, although exposure to adverse living conditions at birth and (or) during upbringing—for example, to poverty, poor housing, or poor nutrition—might explain the high risk for schizophrenia found in immigrants from developing countries,^{7,36} second-generation immigrants from developing countries should have better living conditions than their parents and should thus have lower risks for schizophrenia than their parents, rather than the higher risks generally found in this group.⁷

Social adversity may lead to increased psychosocial stress. Although stress is generally thought to play a precipitating, rather than a causal, role in the development of schizophrenia,⁵² the social defeat hypothesis proposes that stress related to social rank may be particularly harmful, perhaps owing to the risk for social exclusion or outsider status.⁵³ Wicks et al⁵⁴ examined childhood exposure to social adversity, using register-based data from a Swedish national cohort and household indicators similar to those used by Hjern et al.⁴³ Childhood exposure to rental apartments, single-parent households, parental unemployment, and households receiving social welfare were all risk factors for schizophrenia. A dose–response relation was found, with increased risk associated with the number of risk exposures⁵⁴ providing a plausible case for causality. The authors suggested that one possible unifying factor of these indicators might be social exclusion. Such a notion would be compatible with the symptom-formation pathway suggested by the social defeat hypothesis^{5,7} and the results

from animal experiments implicating social isolation.³² In a UK study by Mallett et al,⁵⁵ a single-parent household was also shown to be a risk factor for schizophrenia. In that study, long periods of separation from either or both parents in childhood were associated with a higher risk for schizophrenia in African-Caribbean subjects. In contrast, Bhugra et al⁵⁶ failed to find any group differences in separation from parents or in other social factors in Asian and white first-onset schizophrenia patients in the United Kingdom; however, rates for schizophrenia in Asian individuals are generally lower than rates in African-Caribbean individuals.⁷ An increased risk for schizophrenia is associated with early parental loss, especially before age 9 years, although parental loss may not solely represent environmental factors.⁵⁷ Indeed, genetic predisposition may influence both the type of early environmental stressor the offspring is exposed to and the extent to which the individual is rendered vulnerable by the exposure. Thus, although causality remains difficult to determine, the data on exposure to adversity during upbringing certainly raise questions about the contributory role of the social environment in the development of psychosis in vulnerable or marginalized groups.

Several recent studies have addressed the question of whether childhood abuse (either physical or sexual) is a risk factor for schizophrenia, with somewhat mixed results. That said, it may be difficult to obtain nonbiased information concerning such sensitive experiences. As well, childhood abuse may be a marker for other potentially relevant risk factors, such as family dysfunction. Using information based on forensic reports in Australia, Spataro et al⁵⁸ did not find any increase in adult schizophrenia related to childhood sexual abuse, although abuse that leads to forensic investigation may also result in protective measures being taken. In contrast, Bebbington et al⁵⁹ found that, in the United Kingdom, childhood exposure to events involving victimization (that is, sexual or physical abuse) was strongly related to the presence of psychotic disorder in adulthood. This study did not control for the potential influence of parental mental illness. The Janssen et al⁶⁰ study in The Netherlands used a prospective design that included only subjects with newly emerging psychotic symptoms, thus avoiding potential recall bias. Analyses were adjusted for several potential confounders, including lifetime drug use, unemployment, and parental history of psychiatric treatment. Reported childhood abuse predicted psychotic symptoms in adulthood in a dose–response manner. The authors proposed that persistent stress related to childhood traumatic events can lead to permanent alterations in the hypothalamic–pituitary–adrenal axis, which in turn may result in the dopaminergic dysregulation characteristic of psychosis.⁶⁰ Similarly, Spauwen et al,⁶¹ using data from Germany, found that exposure to psychological trauma in early or middle childhood increased the risk of later psychotic symptoms in a

dose–response manner. Finally, a recent cross-sectional study of child and adolescent referrals in The Netherlands showed that the increased risk of psychotic symptoms found in first-generation immigrant children and adolescents was even greater in families showing signs of dysfunction, such as a disturbed relationship between parent and child, a poor relationship between the adults, or child abuse.⁶² Although the direction of causality concerning family dysfunction remains difficult to resolve, these findings are compatible with results from studies of high-risk adoptees showing that dysfunctional family environments contribute to the development of schizophrenia in adoptees at high genetic risk.⁶³ Moreover, the low rates of schizophrenia found in certain groups, such as Turkish immigrants,⁴² indicate that such factors as family cohesion and social networks may act as buffers in the presence of social adversity.

Neighbourhood Effects

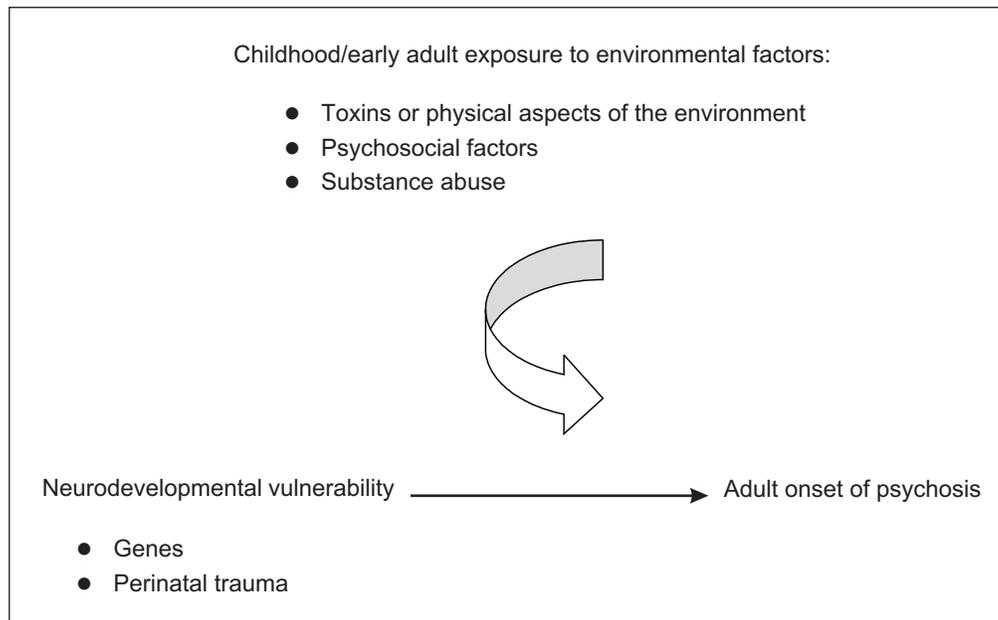
Several studies show that rates of schizophrenia are influenced by neighbourhood or ecologic effects, which implicates the influence of the social or cultural context. In the United Kingdom, Boydell et al¹³ found evidence of an ecologic effect on schizophrenia incidence in electoral wards in Camberwell. Incidence rates associated with nonwhite minority status were lower when the proportion of minority group members residing in an area increased. Greater numbers of minorities presumably confer protection against such adverse aspects of the social environment as discrimination and isolation.¹³ Boydell et al⁶⁴ also examined socioeconomic inequality within electoral wards and found that increased inequality within the ward was related to increasing incidence of schizophrenia, but only in the most socioeconomically deprived wards. Thus the effect of individual levels of social deprivation may be enhanced by neighbourhood characteristics such as lack of social cohesion and social mistrust. Van Os et al⁶⁵ examined neighbourhood variations in schizophrenia incidence, using data from the Maastricht Mental Health case register. The effect of single marital status as a risk factor for schizophrenia was inversely related to the proportion of single and divorced persons living in a given neighbourhood. The authors suggested that premorbid vulnerability to schizophrenia, as indicated by single status, might more readily progress to overt schizophrenia in environments that heighten individual perceptions of social isolation. Further evidence of neighbourhood characteristics as determinants of variations in schizophrenia incidence is provided by the AESOP study of psychosis.⁶⁶ Incidence rates of schizophrenia were found to be greater in Southeast London than in Nottingham and Bristol, even after adjustment for ethnicity.⁶⁶ The authors suggest that the greater rates in Southeast London could be due to “psychotogenic” effects of that environment, including, for example, social capital and neighbourhood deprivation,

although differential exposure to biological factors could not be ruled out.⁶⁶ All in all, the studies that have examined the influence of neighbourhood social contextual effects on schizophrenia incidence remain few in number.⁶⁷ A major challenge in such studies is the separation of individual-level and neighbourhood-level effects and the ever-present issue of causality.

Does the Urban Effect in Schizophrenia Lend Support to the Social Causation Hypothesis?

The AESOP study findings of greater incidence rates in Southeast London, an area that is highly urbanized, are well in line with Danish studies indicating a dose–response increase in schizophrenia risk associated with urban birth and (or) urban upbringing.^{68,69} A recent review suggests that the rate of schizophrenia in urban areas is about twice that in rural areas, with “urban” variously defined across studies as density of people, density of addresses, “large” compared with “small,” and so forth.⁶ None of the known risk factors for schizophrenia adequately explain the urban effect.⁷⁰ Some findings suggest that aspects of the social environment may be relevant. Rates of nonclinical psychosis-like phenomena are more prevalent in urban areas,⁷¹ suggesting that community levels of psychotic symptoms and the prevalence of psychotic disorder are closely linked. Variations in community levels of nonclinical psychosis-like phenomena could be attributable to factors in the social environment. Further, the fact that the urban effect appears to be cumulative during upbringing⁶⁸ suggests the importance of repeated or continuous exposure that gives rise to an enduring liability, rather than an exposure that acts as a precipitant. Also, the urban effect is not mediated by obstetric complications or childhood SES, that is, maternal education.⁷² The urban effect also shows some specificity for schizophrenia, as shown in a recent register-based study in Sweden, where increasing levels of urbanization had a somewhat greater impact on risk for schizophrenia than on risk for depression.⁷³ In a study from The Netherlands, urbanization and familial liability both contributed independently to the risk for psychosis, with evidence of biological synergism between these factors.⁷⁴

Curiously, the urban effect has also been found in Uganda, where psychotic experiences were more prevalent in an urban, compared with a rural, setting⁷⁵—although the physical characteristics of the urban setting (Mbarara town) would not be regarded as urban by developed-country standards. These results from Uganda suggest that “urban” may be rooted in an individual’s mental environment rather than in any physical characteristic. Nevertheless, it may be premature to assume that the urban effect is consistent across settings. A study conducted in Queensland, Australia, found that urban birth was not associated with increased risk for psychosis.⁷⁶ These

Figure 1 Pathways to schizophrenia: a biopsychosocial model

important negative findings raise questions concerning possible candidate mechanisms. Thus physical features of the environment, including climate and sunlight, cannot yet be excluded. This study also failed to find an increased risk of schizophrenia in second-generation migrants to Australia.⁷⁶

More recent studies in Denmark also cast doubt on whether urban findings should be interpreted solely in terms of social factors. A cohort study in Denmark that included over 5 million people found no evidence of time trends in the urban–rural differences in schizophrenia risk during the period 1910 to 1986,⁷⁷ in contrast to previous findings from Finland⁷⁸ and The Netherlands⁷⁹ that showed an increase in the urban effect over time. The stability of the urban effect over time found in Denmark is puzzling because most factors related to the environment, whether social or physical, would undergo major changes during this period. Also, in a separate study of urbanization in Denmark,⁸⁰ Pedersen and Mortensen found that some of the increased risk for schizophrenia associated with urban birthplace was independently related to the birthplace of the nearest older sibling. This important finding indicates that the factors responsible for the urban birth effect may be rooted in families, as well as in individuals or aspects of the environment. Although social factors may be implicated in the urban effect, it may be premature to attribute the urban effect solely to social factors.

The Evidence for Social Causation: Where Do We Go From Here?

Variations in schizophrenia risk according to ethnicity, social adversity, and urbanization lend credibility to a role for the social environment in the etiology of schizophrenia. Moreover, nonclinical levels of psychotic experience show similar between-population patterns of variation. Collectively, this body of evidence, arising primarily from studies conducted in Europe, suggests that factors operating on the societal, neighbourhood, and family–individual level contribute to enduring liabilities that may lead to manifest schizophrenia. Although some would argue that psychosocial factors merely act as precipitants of onset or relapse,³ the dose–response effect shown by several of the risk factors reviewed here^{41,54,60,61,68} weighs strongly in favour of causality rather than merely statistical association.⁸¹ Nevertheless, none of these findings provide support for the notion that some cases of schizophrenia are entirely socially determined. Thus the etiological trajectory leading to schizophrenia might best be described by an integration of biological and social perspectives (Figure 1). As indicated by this model, a contributory role for nonsocial environmental factors such as climate, exposure to toxins, pollution, or viruses cannot yet be excluded.

A major challenge for the social causation hypothesis is the isolation of the relevant exposure variable(s). Most of the exposures thus far implicated (for example, stress and social defeat) are highly prevalent, difficult to measure, and

somewhat overlapping. Many situations involving social defeat are also highly stressful, and vice versa. Psychological trauma, as in the study by Spauwen et al,⁶¹ often involves victimization and social defeat. Social risk factors thus tend to contain various components, making it difficult to tease out the relevant exposure variable(s). Specificity remains a problem because stress and social deprivation during upbringing may lead to many different forms of mental illness and not solely to psychosis. Nevertheless, although specificity would be a strong argument in favour of social causation, its absence does not necessarily negate causation.⁸¹

Thus far, the strongest evidence for the social causation of schizophrenia is provided by migrant studies, as indicated by the effect strength and its consistency across studies and also by the plausibility of the mechanisms proposed for symptom development.⁷ The markedly elevated incidence of schizophrenia found in ethnically diverse first- and second-generation immigrants with “black” skin colour in the United Kingdom^{7,37} is difficult to explain in terms of any single biological or genetic factor. Although social defeat and discrimination are tenable explanations, such experiences are nevertheless highly subjective and difficult to measure on an individual level without recall bias. The study of defeated populations is perhaps currently still the most fruitful line of inquiry.⁵ Interestingly, although African-Caribbean individuals report similar numbers of adverse life events as do white British individuals, African-Caribbeans are more likely to interpret these events in terms of ethnic discrimination.⁸² Negative attributes about the self related to ethnic discrimination may be one part of the process whereby social perceptions are transformed into delusions or abnormal thoughts.⁸³ Nevertheless, psychotic symptoms could also predispose individuals to increased perceptions of discrimination. Cross-sectional studies of discrimination and psychotic symptoms,⁸⁴ although suggestive, cannot resolve the issue of causality. Thus far, only one study has examined the temporal relation between discrimination and the development of psychotic symptoms, albeit not in a sample of ethnic minorities.³⁵

Indeed, the biological plausibility of the notion that social factors such as discrimination can lead to a chronic disease of the brain is primarily based on results from animal experiments, and animal models may not provide satisfactory analogues for the complexity of the human environment. Although the alterations in dopaminergic sensitivity seen in schizophrenia patients and in animals exposed to social defeat are similar, very few human studies of social defeat have been conducted. Studies in humans would need to differentiate between the experience of social defeat and behavioural reactions to defeat such as substance abuse, which is also strongly related to schizophrenia.^{44,45} Simulated social-defeat paradigms performed on humans might help control for such confounders,

provided that ethical concerns were adequately addressed. Neuroimaging studies could explore the human brain’s response to social defeat and potential between-population differences. Although laboratory simulations may demand considerable ingenuity, the exposure variable represented by social defeat and (or) discrimination may be more readily deconstructed in an experimental setting than the variables of urbanization or socioeconomic deprivation.

Although the task of specifying the causal mechanisms that underlie the association between socioenvironmental factors and schizophrenia may pose an enormous challenge, the clinical implications of such an effort may well be far-reaching. Identifying the genes responsible for schizophrenia will not likely lead to any viable prevention strategies in the near future. In contrast, identifying aspects of the social environment that are causally related to schizophrenia and accessible for targeting by intervention programs may lead to risk reduction. Therefore, the role of social environmental factors merits further attention in schizophrenia research.

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Résumé : La contribution des facteurs sociaux au développement de la schizophrénie : un examen des résultats récents

Objectif : Cette étude vise à examiner les données probantes récentes suggérant que les facteurs sociaux ont un lien de causalité au développement de la schizophrénie.

Méthode : Une recherche systématique de MEDLINE a été menée pour repérer les études pertinentes. La recherche se limitait aux études révisées par les pairs et aux articles parus dans des revues en anglais depuis 1996. Les études étaient incluses si elles utilisaient des critères diagnostiques normalisés pour la schizophrénie ou des instruments d'évaluation normalisés pour les symptômes psychotiques.

Résultats : Les études d'émigrants en Europe occidentale soutiennent indéniablement la notion selon laquelle les facteurs sociaux contribuent au développement de la schizophrénie. Des observations comme les risques excessivement élevés de schizophrénie chez les immigrants de deuxième génération sont difficiles à expliquer uniquement par des facteurs biologiques ou génétiques. Un nombre croissant d'études impliquent l'exposition à l'adversité sociale dans l'enfance comme facteur de risque de la schizophrénie, bien que peu d'études aient utilisé des méthodes prospectives. L'incidence croissante du risque de schizophrénie associé avec une naissance et (ou) une éducation en milieu urbain suggère des causes sociales possibles, mais ces résultats sont plus ambigus. Jusqu'ici, aucune étude n'a exploré les mécanismes réels par lesquels l'exposition à des facteurs sociaux pourrait produire des symptômes psychotiques, bien que les expériences sur les animaux suggèrent que le rejet social ou l'exclusion sociale puisse causer un dérèglement de la dopamine ou une sensibilisation à celle-ci.

Conclusions : Les données probantes qui s'accumulent suggérant un rôle des facteurs sociaux dans le développement de la schizophrénie proviennent principalement d'études menées auprès de migrants en Europe. Les mécanismes par lesquels les facteurs sociaux exercent leur influence demeurent inconnus. Les futures recherches sur les causes sociales devraient clarifier la relation temporelle entre l'exposition au rejet social et (ou) à l'exclusion sociale et le développement de symptômes psychotiques.