Review Article

Ethnic origin and increased risk for schizophrenia in immigrants to countries of recent and longstanding immigration

Dealberto M-J. Ethnic origin and increased risk for schizophrenia in immigrants to countries of recent and longstanding immigration.

Objectives: Compare the risk for schizophrenia in immigrants to countries of recent and longstanding immigration. Compare prevalence and incidence rates in black subjects under different conditions.

Method: An electronic literature search was complemented by review articles and cross-references. Studies reporting standard diagnosis and incidence or prevalence rates were included.

Results: Immigrants had an increased risk for schizophrenia in countries of longstanding immigration, but with lower risk ratios than in those of recent immigration. The risk was higher in black immigrants and the black population living in the United States. But incidence and prevalence rates in Africa and the Caribbean were similar to those of international studies.

Conclusion: Comparing the most recent generation of immigrants with descendants of previous ones may account for the lower risk ratios observed in countries of longstanding vs. recent immigration. Two neurobiological hypotheses are proposed to explain the epidemiological findings in black populations and in immigrants.

Key words: schizophrenia; immigration; ethnicity; vitamin D; autism

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Accepted for publication December 17, 2009

Summations

• In countries of both recent and longstanding immigration schizophrenia was more frequent in immigrants than in native-born populations, and especially so in dark skinned immigrants.
• This comparative review implies a hidden epidemic of schizophrenia and psychosis in immigrants to North America and an unrecognized epidemic of schizophrenia in black subjects living in North America.
• The hypothesis of vitamin D deficiency can explain the higher risk in dark skinned compared with light skinned subjects; the hypothesis of epigenetic mechanisms can explain the higher risk observed overall in all immigrants, independent of skin color. Both hypotheses combined can explain why the risk is the highest in dark skinned immigrants to Northern latitudes.

Considerations

• The studies included were mainly from Western countries. No data were available for most countries with the highest numbers or highest proportions of immigrants.
• Because of the lack of recent data in countries of longstanding immigration, this review compared studies conducted with very different methodologies. The conclusions of high rates of schizophrenia and psychosis in immigrants to North America and of high rates of schizophrenia in black subjects living in North America should be verified by specially designed epidemiological studies including objective measurements of skin color.
• The hypotheses proposed by this review should be tested in neurobiological and epidemiological studies.
Introduction

Immigration on a large scale has dramatically increased in the last century and this has had unexpected serious consequences on mental health. There is mounting evidence of a psychosis epidemic (1) as most epidemiological studies have observed an abnormally high occurrence of schizophrenia and psychosis in immigrants compared with the native-born population. The meta-analysis of Cantor-Graae and Selten (2) found that immigrants were 2.9 times more likely to develop schizophrenia than were native-born subjects. Two reviews of both incidence and prevalence data reported similarly higher risks in immigrants: the median migrant to native-born ratio for schizophrenia was 4.6 in incidence studies (3) and 1.8 in prevalence studies (4). The excess risk differed markedly according to ethnic origin, as it was much more elevated in black immigrants than in their white or non-white non-black counterparts. It is remarkable that the increased risk for schizophrenia was also observed in the second generation of immigrants (2). Increased risks in immigrants have similarly been observed on both sides of the schizophrenia spectrum: in other types of psychosis (5–8) and in neurodevelopmental disorders such as autism in children born to immigrant parents (9–18). However, no increased risk has been found for other mental disorders.

Although almost all the recent data on the relationship between schizophrenia rates and migrant status come from Europe, the earliest studies were performed in North America. The pioneering work of Ødegaard (19) was followed by that of Malzberg who examined data both from New York State (New York City was the port of entry for most immigrants) and Canada (where countrywide mental hospital statistics were available). However the differences in schizophrenia rates between foreign-born and native-born populations decreased over time, and became non-significant in analyses taking into account socioeconomic status (20). Subsequently, this topic was abandoned for decades in North America. Despite reporting increased rates in persons born in the new country to foreign-born parents (21, 22), the early authors did not consider that, when comparing rates in foreign-born and native-born populations, they were in fact comparing rates in the last arrived generation of immigrants (i.e., first generation) and descendants of the previous ones (i.e., second and later generations). To date no study has focused on possible differences regarding the increased risk for schizophrenia in foreign-born subjects according to the immigration pattern, whether recent or longstanding.

One constant finding in the epidemiology of schizophrenia in immigrants is the particularly elevated risk in black immigrants. However it is difficult to separate the immigrant effect from the ethnic origin effect. The finding by epidemiological studies conducted in the 1990s in the Caribbean (23–25) of rates similar to those of white British in the UK stressed the importance of the immigrant effect. But to date no author has compared rates in black subjects according to whether they are recent immigrants, long established inhabitants, or native populations.

Aims of the study

The first aim of this article is to review international data on the increased risk for schizophrenia in immigrants focusing on an expected difference between countries of recent and longstanding immigration. It was hypothesized that the risk in foreign-born compared with native-born populations would be less important in countries largely populated by immigrants because of the ‘dilution’ effect when comparing rates between foreign-born subjects and the offspring of earlier immigrants. The second aim is to separate immigrant status and ethnic origin by comparing data in recent black immigrants, in black subjects in countries where they have been established for centuries (Caribbean and US) and in black populations in Africa.

Material and methods

Comparison between countries of recent and longstanding immigration

This review researched the scientific literature on the relationship between schizophrenia and immigrant status following recommendations for reporting observational studies in epidemiology (26). A Medline search limited to articles published before June 2009 (without early date constraints) and to human subjects was performed using the keywords (schizophren* or psychosis) and (epidemiology or incidence or prevalence) and (ethnic* or skin color or immigrant or immigration). It yielded 923 articles in English and 77 in other languages. A Scopus search performed using these keywords yielded 78 articles.

Titles and abstracts, when available, were reviewed to exclude irrelevant studies. Then the remaining articles were identified according to the inclusion criteria detailed below. These searches were complemented by references in the already
cited meta-analysis (2), two recent systematic reviews of incidence (3) and prevalence (4), review articles on the epidemiology of schizophrenia published in journals or in books (27–33), review articles on the excess risk of schizophrenia in immigrants (34–47), government sponsored reports on the mental health of immigrants (48–50), plus cross-references from retrieved articles. The same criteria were applied to these studies. When several articles presented the same data, the most informative study was chosen. Special attention was given to articles in languages other than English.

Inclusion criteria were: i) data pertinent to external migration, i.e., from one country to another one; ii) clinical diagnosis or diagnosis criteria for schizophrenia or dementia praecox; iii) incidence rates (first contact or first admission) for schizophrenia and schizophrenic disorders in the immigrant and in the native-born population, which allowed the calculation of rate ratios.

This review included all types of immigrants (e.g., work, study, economic reasons, family unification, refugee status) and did not differentiate between these groups. No data were available for illegal immigrants. Although immigrants are at increased risk for other types of psychosis, this review was restricted to schizophrenia and schizophrenic disorders. As the relationship to immigration was similar in men and women (2), data for both genders were combined for ease of presentation.

Countries in the selected studies were classified into two groups according to the proportion of the autochthon population: more or less than 50%. The group with an autochthon proportion of more than 50% was comprised of European countries (Denmark, the Netherlands, Sweden, United Kingdom) for which immigration on a large scale is a relatively recent phenomenon. In this article they are referred to as ‘countries of recent immigration’. In contrast, the countries in the other group (Australia, Canada, Israel, US) were populated by successive waves of immigrants, reducing the autochthon population to only a fraction of the total: 2.0% in the US, 2.3% in Australia, 3.8% in Canada (51). According to recent demographic data foreign-born subjects constituted 12–35% of the total population in these countries and the percentages were still more striking when one considers together the first and second generation of immigrants: 70% in Israel (52), 44% in Australia (53), 40% in Canada (51) and almost 23% in the US (54). Countries in this second group are referred to as ‘countries of longstanding immigration’. Population and immigration data for countries in both groups are presented in Fig. 1.

No systematic data were available for other countries and, in particular, for four of the five countries with the largest number of international immigrants: Russian Federation, Germany, France, Saudi Arabia (the US being the first), and for four of the five countries with the highest proportion of immigrants: United Arab Emirates, Kuwait, Singapore, Jordan (Israel being the fourth) (54).

The estimates for countries of recent immigration were those given by Cantor-Graae and Selten (2). This meta-analysis included one study from Australia, a country of longstanding immigration (55); this could only lessen the expected dissimilarity between both groups of countries. Recent studies in Australia, Canada and the US were almost non-existent, so it was necessary to resort to early data and to retrieve articles published before systematic inclusion in Medline or Scopus. Only first admission rates were given in these early studies. The earliest available data for countries of recent immigration were published in the late 1970s and 1980s (2).

Because of the differences in methodology between the studies, no statistical testing was performed in this review.

Schizophrenia rates in black populations

The second aim of the study stemmed from the greatly increased risk for schizophrenia in black immigrants. Black ethnicity in this article refers to persons with mainly African lineage. Dark skin refers to skin color.

The scientific literature was searched for data providing rates in black subjects. Three searches were performed in Medline for studies published before June 2009, limited to humans. For studies in African countries the keywords were (schizophren* or psychosis) and (epidemiology or prevalence or incidence) and (Africa*). The search yielded 624 studies in English and 21 in other languages. For studies in the Caribbean the keywords were (schizophren* or psychosis) and (epidemiology or prevalence or incidence) and Caribbean. This search yielded 227 studies in English and 12 in other languages. For studies in black populations in the US the keywords were (schizophren* or psychosis) and (epidemiology or prevalence or incidence) and (race or ethnicity or skin color) and (United States or USA). This search yielded 747 studies in English and six in other languages. Special attention was again given to studies in language other than English. These searches were
complemented by Scopus searches (126, 88 and 78 articles retrieved respectively).

Titles and abstracts, when available, were reviewed to reject any irrelevant studies. The remaining articles were identified according to the criteria described below. These searches were complemented by review articles pertaining to Africa (56), the Caribbean (57) and African Americans in the US (58–66).

Inclusion criteria were: i) clinical diagnostic or diagnosis criteria for schizophrenia or dementia praecox; ii) a) incidence rates (first contact or first admission) for studies in the Caribbean; ii) b) because of the paucity of incidence data in Africa, prevalence rates when rate and either numerator or denominator were given; ii) c) incidence rates (first contact or first admission) in white and black populations in the US allowing the calculation of rate ratios.

Suriname was included in the Caribbean following its broad definition as the chain of islands and the American coast along the Caribbean Sea. Because the main interest resided in black ethnicity, only Caribbean countries with populations mainly of this ethnicity were included.

Results

Increased risk for schizophrenia in immigrants

European countries. Studies in Northern Europe have consistently observed an increased risk for schizophrenia in immigrants. The meta-analysis by Cantor-Graae and Selten (2) carefully selected 18 studies, 17 of which were from Northern Europe: 12 from the UK, three from the Netherlands, one from Sweden, one from Denmark. The pooled estimate of the risk associated with immigration was 2.7 (95% CI: 2.3–3.2) for the first generation and 4.5 (95% CI: 1.5–13.1) for the second generation compared with the native-born population. More recent studies report similar findings. In Britain, black and ethnic minority groups were 3.6 times more at risk than native white subjects (8). In the Netherlands, a follow-up study (67) confirmed results of a
Immigration, ethnicity and schizophrenia

previous report (68) showing particularly increased risks in immigrants from Suriname and Morocco both for the first and second generations.

Countries of longstanding immigration: Australia, Canada, Israel and US Rates in countries of longstanding immigration for foreign-born and native populations are presented in Table 1.

Two early studies in Australia found overall a moderately increased risk for schizophrenia in immigrants (55, 69). Similar results were observed in Canada, with a risk ratio ranging between 1.2 and 1.8 (70–72).

Table 1. Incidence rates (per 100 000 persons) of schizophrenia in native-born and foreign-born subjects in countries of longstanding immigration

<table>
<thead>
<tr>
<th>Country</th>
<th>First author, publication year</th>
<th>Type of study</th>
<th>Location case ascertainment</th>
<th>Date of study</th>
<th>Incidence in native-born subjects</th>
<th>Incidence in foreign-born subjects</th>
<th>Ratio foreign-born/native-born</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>Krupinski, 1965 (69)</td>
<td>Hospital study</td>
<td>Victoria first admissions to hospital for schizophrenia</td>
<td>1962</td>
<td>M 24.0/F 30.6</td>
<td>Britain, M 21.9/F 18.2</td>
<td>M 0.9/F 0.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>W Europe, M 59.3/F 53.1</td>
<td>M 2.4/F 1.7</td>
</tr>
<tr>
<td></td>
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<td></td>
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<td></td>
<td>E Europe M, 102.9/F 96.4</td>
<td>M 4.3/F 3.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>S Europe M, 44.6/F 48.8</td>
<td>M 1.9/F 1.6</td>
</tr>
<tr>
<td>Australia</td>
<td>Krupinski, 1980 (55)†</td>
<td>Hospital study</td>
<td>Victoria first admissions to hospital for schizophrenia</td>
<td>1970–1972</td>
<td>M 20/F 21</td>
<td>Britain, M 28/F 16</td>
<td>M 1.4/F 0.8</td>
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<td></td>
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<td></td>
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<td></td>
<td>Germany M 51/F 49</td>
<td>M 2.6/F 2.3</td>
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<td></td>
<td>Poland M 82/F 91</td>
<td>M 4.1/F 4.3</td>
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<td></td>
<td></td>
<td>Italy M 43/F 31</td>
<td>M 2.2/F 1.5</td>
</tr>
<tr>
<td>Canada</td>
<td>Malzberg, 1963 (70)</td>
<td>Administrative data</td>
<td>Canada first admissions for dementia praecox to all mental institutions</td>
<td>1950–1952</td>
<td>28.2</td>
<td>49.8</td>
<td>1.8</td>
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<td></td>
<td>9031/104929</td>
<td>1686/1961792</td>
</tr>
<tr>
<td>Canada</td>
<td>De Hesse, 1967 (71)</td>
<td>Administrative data</td>
<td>Canada except Quebec first admissions for dementia praecox to all mental institutions</td>
<td>1961</td>
<td>29.1</td>
<td>33.8</td>
<td>1.2</td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>3919/1961 census</td>
<td>3919/1961 census</td>
</tr>
<tr>
<td>Canada</td>
<td>Smith, 2006 (72)</td>
<td>Archival data</td>
<td>British Columbia first admissions for schizophrenia and schizophrenia-related disorders</td>
<td>1902–1905</td>
<td>22.9</td>
<td>27.5</td>
<td></td>
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<td></td>
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<td>1906–1909</td>
<td>29.9</td>
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<td>1910–1913</td>
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<td></td>
<td></td>
<td>807/NA</td>
<td>44.4</td>
</tr>
<tr>
<td>Israel</td>
<td>Weiser, 2008 (73)</td>
<td>Cohort study: subjects screened by Draft Board</td>
<td>Israel first admission to hospital for schizophrenia</td>
<td>1966/1961792</td>
<td>284/104638</td>
<td>46/22589</td>
<td>1.5</td>
</tr>
<tr>
<td>USA</td>
<td>Malzberg, 1935 (21)</td>
<td>Administrative data</td>
<td>New York State all first admissions to hospital for dementia praecox (white population)</td>
<td>1929–1931</td>
<td>22.2</td>
<td>32.8</td>
<td>1.5</td>
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<td>6962/NA</td>
<td>6962/NA</td>
</tr>
<tr>
<td>USA</td>
<td>Faris, 1939 (84)</td>
<td>Administrative data</td>
<td>Chicago all first admissions to hospital for schizophrenia (white population)</td>
<td>1922–1934</td>
<td>26.1</td>
<td>38.1</td>
<td>1.5</td>
</tr>
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<td></td>
<td></td>
<td>10575/NA</td>
<td>10575/NA</td>
</tr>
<tr>
<td>USA</td>
<td>Malzberg, 1955 (100)</td>
<td>Administrative data</td>
<td>New York State all first admissions to hospital for dementia praecox (white population)</td>
<td>1939–1941</td>
<td>30.4</td>
<td>42.1</td>
<td>1.4</td>
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<td></td>
<td>10113/NA</td>
<td>10113/NA</td>
</tr>
<tr>
<td>USA</td>
<td>Malzberg, 1964 (75)</td>
<td>Administrative data</td>
<td>New York State all first admissions to hospital for dementia praecox (white population)</td>
<td>1949–1951</td>
<td>41.3</td>
<td>52.7</td>
<td>1.3</td>
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<td></td>
<td>13802/NA</td>
<td>13802/NA</td>
</tr>
<tr>
<td>USA</td>
<td>Malzberg, 1969 (76)</td>
<td>Administrative data</td>
<td>New York State all first admissions to hospital for dementia praecox (white population)</td>
<td>1980–1981</td>
<td>44.8</td>
<td>48.5</td>
<td>1.1</td>
</tr>
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<td></td>
<td></td>
<td>10355/NA</td>
<td>10355/NA</td>
</tr>
</tbody>
</table>

All rates are age-standardized except the cohort study by Weiser.
†This study was included in the meta-analysis by Cantor-Graae and Selten (2).
‡Hazard ratio adjusted for socioeconomic status and gender.
§Offspring of native-born parents.
In a very large sample of 661,792 Israeli adolescents followed for 7.7 years by Weiser et al. (73), the risk for schizophrenia was similarly increased in both the first generation (Hazard ratio HR = 1.6) and the second generation (HR = 1.4 for one immigrant parent, 1.6 for two immigrant parents) compared with the offspring of native-born subjects. The Jerusalem Perinatal cohort was not included in this review as it did not give rates for foreign-born subjects (74).

In New York State, Malzberg minutely documented higher risks for a first admission for dementia praecox in foreign-born compared with the native-born subjects. In the white population, the rates increased between 1930 and 1960 in both groups but more so in the native-born persons, as reflected in the progressive decrease of the rate ratio between foreign-born and native-born population: 1.5 in 1930, 1.4 in 1940, 1.3 in 1950, then 1.1 in 1960 (21, 75, 76). Probably the only study that has compared black immigrants to the native black population found higher rates in the foreign-born subjects with a ratio equal to 1.3 (77). Socioeconomic conditions were not responsible for this difference, as census data indicated that the foreign-born males, who were coming mainly from the Caribbean, were living in more favorable circumstances than their native-born counterparts.

Low rates in Africa. Africa is an ethnically very diverse continent with several thousand ethnic groups, and the majority of its countries are mainly inhabited by peoples of African origin. Few epidemiological studies have been conducted in Africa. Those selected for this review found prevalence rates between 0.6 and 8 per 1000 (see Table 2). These values were in the low medium range of the estimates given by Saha et al. (4) with a lifetime median value equal to 4.0 per 1000 (mean equal to 5.5 per 1000).

Rates in the Caribbean not elevated. The Caribbean is an ethnically very diverse ensemble of countries in which the native populations were almost decimated by the white colonization. They were populated by white settlers who imported under coercion black slaves from 1500 to 1800 then, after the abolition of slavery, by indentured Indian workers, followed by Chinese traders. People with black ancestry represent the majority of the population in most of these countries.

<table>
<thead>
<tr>
<th>Country</th>
<th>First author, publication year</th>
<th>Urban/rural</th>
<th>Date of study</th>
<th>Age</th>
<th>Cases/denominator</th>
<th>Type of prevalence</th>
<th>Prevalence rates and criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudan</td>
<td>Baasher, 1961 (142)</td>
<td>Rural</td>
<td>1961</td>
<td>All</td>
<td>13/1860</td>
<td>Point</td>
<td>7.0</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Giel, 1969 (143)</td>
<td>Small town</td>
<td>1967</td>
<td>All</td>
<td>1/384 + 337</td>
<td>Lifetime</td>
<td>1.4</td>
</tr>
<tr>
<td>Ghana</td>
<td>Sikanartey, 1984 (144)</td>
<td>Urban</td>
<td>1978</td>
<td>15+</td>
<td>28/34 018</td>
<td>2 weeks</td>
<td>0.62 ICD-8</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Bondestam, 1990 (146)</td>
<td>NA</td>
<td>1988</td>
<td>15+</td>
<td>NA/10 776</td>
<td>Point</td>
<td>1.0</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Awas, 1999 (130)</td>
<td>Rural</td>
<td>1995–1996</td>
<td>15+</td>
<td>9/501</td>
<td>1 month</td>
<td>6 ICD-10</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Kebede, 1999 (131)</td>
<td>Urban</td>
<td>1994</td>
<td>15+</td>
<td>NA/1418</td>
<td>1 month</td>
<td>3 ICD-10</td>
</tr>
</tbody>
</table>
Incidence rates for several Caribbean countries are displayed in Table 3. The only outlier was found in an early study (78) and this result was not confirmed by a later study with a superior methodology (24). The other incidence rates range from 10.8 to 28.2 per 100 000 for restrictive criteria of schizophrenia, from 16.1 to 31.7 per 100 000 for broad criteria. These values are close to the estimates of 15.2 per 100 000 for the median and 23.7 per 100 000 for the mean given by McGrath et al. (3) in a systematic review of studies using mainly broad criteria.

Three studies in English speaking Caribbean countries: Jamaica (23), Trinidad and Tobago (24) and Barbados (25) used the same methodology as British ones and found rates similar to those observed in native white British in the UK. Two studies in Dutch speaking Suriname similarly reported rates comparable to those observed in native Dutch in the Netherlands (79, 80).

Rates in the US. The rates observed in black subjects in the US contrast with those observed in black subjects in Africa and the Caribbean. The rates for black and white populations and their ratios are presented in Table 4.

Malzberg (81–83) reported rates for first admission for schizophrenia in the black and white populations of New York State for 1929–1931, 1939–1941 and 1949–1951. In all three periods, the rates were higher for the black subjects and the ratio increased across time from 2.0 to 2.3 to 2.6. First admission rates in Chicago (84) and in the states of Ohio (85–87), Virginia (88) and California (86) observed similar differences, the only exception being found in Texas (89). In a mostly rural environment, Monroe County in New York State, the treated incidence rates, including in-patients and out-patients, were more than two times higher in black than white subjects (90).

These results are apparently contradicted by two large epidemiological studies. The National Comorbidity Survey (91) found non-significant differences between the black and white populations, with odds ratios for black ethnicity equal to 1.3 (95% CI: 0.7–2.6) for the Composite International Diagnostic Interview (CIDI) diagnostic of narrowly defined psychosis and 1.9 (95% CI: 0.9–4.0) for the clinician diagnosis of non-affective psychosis. The statistical power of this study was 25% for CIDI and 77% for clinician diagnosis. The Epidemiological Catchment Area study (92) with 20 291 subjects at five sites observed a significantly higher prevalence of schizophrenic disorders in black subjects compared to their white counterparts: 21 and 14 per 1000, respectively, for 1 year prevalence, with a crude RR equal to 1.5. This relationship was not significant when age, sex, socioeconomic status and marital status were considered; this was probably because of overadjustment, as current socioeconomic status and marital status might be a consequence of the disorder. As suggested by Williams (62) another explanation is the possible higher rate of non-respondents in black young men.

It is important to discuss these epidemiological results, as they have been relied upon to explain the excess of black patients admitted in the US for schizophrenia by misdiagnosis, racism or low socioeconomic status. Nevertheless the figures are overwhelming. In a nationally representative database of admissions to state and county hospitals (93), the rates of hospitalization for schizophrenia from 1974 to 1986 remained at very high levels in

Table 3. Incidence rates (per 100 000 persons) of schizophrenia in the Caribbean

<table>
<thead>
<tr>
<th>Country</th>
<th>First author, publication year</th>
<th>Date of study</th>
<th>Methodology criteria</th>
<th>Age range adjustment</th>
<th>Cases/denominator</th>
<th>Incidence rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trinidad and Tobago</td>
<td>Neehall, 1991 (78)</td>
<td>1986</td>
<td>Hospital in-patient</td>
<td>15+</td>
<td>49/100 159</td>
<td>48.9</td>
</tr>
<tr>
<td>Jamaica</td>
<td>Hickling, 1995 (23)</td>
<td>1992</td>
<td>First contact CATEGO</td>
<td>15–54 Age-adjusted</td>
<td>320/1,350 000</td>
<td>23.6 (broad definition)</td>
</tr>
<tr>
<td>Trinidad and Tobago</td>
<td>Bhugra, 1996 (24)</td>
<td>NA</td>
<td>First contact CATEGO</td>
<td>15–54 Age-adjusted</td>
<td>285/1,350 000</td>
<td>20.9 (restrictive definition)</td>
</tr>
<tr>
<td>Barbados</td>
<td>Mahy, 1999 (23)</td>
<td>1994–1995</td>
<td>First admission to hospital for schizophrenia or schizophreniform disorder DSM-III-R</td>
<td>15–54 Age-adjusted</td>
<td>73/453 384 PY</td>
<td>16.1 (schizophrenia and schizophreniform disorders)</td>
</tr>
<tr>
<td>Surinam</td>
<td>Hanoeman, 2002 (79)</td>
<td>1992–1993</td>
<td>First contact rate CATEGO</td>
<td>15–54 Age-adjusted</td>
<td>49/453 384 PY</td>
<td>10.8 (schizophrenia)</td>
</tr>
<tr>
<td>Surinam</td>
<td>Selten, 2005 (80)</td>
<td>1997–1999</td>
<td>First contact rate for schizophrenia or schizophreniform disorder DSM-IV</td>
<td>15–54 Age-adjusted</td>
<td>64/NA</td>
<td>17.7 (schizophrenic disorders)</td>
</tr>
</tbody>
</table>

PY, person years.

Immigration, ethnicity and schizophrenia
dealberto

Table 4. First admission and first contact rates (per 100 000 persons) of dementia praecox or schizophrenia in the US according to ethnic origin

<table>
<thead>
<tr>
<th>First author, publication year</th>
<th>Case ascertainment location</th>
<th>Date of study</th>
<th>Age adjustment</th>
<th>White population</th>
<th>Black population</th>
<th>Ratio black/white</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malzberg, 1935 (81)</td>
<td>First admission to mental hospitals New York State</td>
<td>1929–1931</td>
<td>Yes</td>
<td>25.7</td>
<td>51.1</td>
<td>2.0</td>
</tr>
<tr>
<td>Faris, 1939 (84)</td>
<td>First admission to major public and private hospitals Chicago</td>
<td>1932–1934</td>
<td>No</td>
<td>32.7</td>
<td>41.4</td>
<td>1.3</td>
</tr>
<tr>
<td>Malzberg, 1953 (82)</td>
<td>First admission to mental hospitals New York State</td>
<td>1939–1941</td>
<td>Yes</td>
<td>32.9</td>
<td>76.1</td>
<td>2.3</td>
</tr>
<tr>
<td>Frumkin 1954 (85)</td>
<td>First admission to state mental hospitals Ohio</td>
<td>1949</td>
<td>No</td>
<td>8.1</td>
<td>18.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Wilson, 1957 (88)</td>
<td>First admission to state hospitals Virginia</td>
<td>1920</td>
<td>No</td>
<td>6.4</td>
<td>12.0</td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1930</td>
<td></td>
<td>9.4</td>
<td>16.1</td>
<td>1.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1940</td>
<td></td>
<td>9.0</td>
<td>10.4</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1950</td>
<td></td>
<td>6.4</td>
<td>14.2</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1955</td>
<td></td>
<td>7.2</td>
<td>21.7</td>
<td>3.0</td>
</tr>
<tr>
<td>Malzberg, 1959 (83)</td>
<td>First admission to mental hospitals New York State</td>
<td>1949–1951</td>
<td>Yes</td>
<td>42.7</td>
<td>109.0</td>
<td>2.6</td>
</tr>
<tr>
<td>Jaco, 1960 (89)</td>
<td>First admission to public and private psychiatric facilities, first contact with private psychiatrists Texas</td>
<td>1950–1952</td>
<td>Yes</td>
<td>38†</td>
<td>31</td>
<td>0.8</td>
</tr>
<tr>
<td>Lazarus, 1963 (86)</td>
<td>First admission to state hospitals for mental disease Ohio (subjects aged 20–59)</td>
<td>1948–1952</td>
<td>Yes</td>
<td>M 22/F 28†</td>
<td>M 53/F 61§</td>
<td>M 2.4/F 2.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1949–1951</td>
<td></td>
<td>M 27/F 35†</td>
<td>M 67/F –§</td>
<td>M 2.5/F –</td>
</tr>
<tr>
<td></td>
<td>First admission to state hospitals for mental disease California (subjects aged 20–59)</td>
<td>1948–1952</td>
<td>Yes</td>
<td>M 22/F 28†</td>
<td>M 53/F 61§</td>
<td>M 2.4/F 2.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1949–1951</td>
<td></td>
<td>M 27/F 35†</td>
<td>M 67/F –§</td>
<td>M 2.5/F –</td>
</tr>
<tr>
<td>Locke, 1965 (87)</td>
<td>First admission to public mental hospitals Ohio (subjects aged 15–64)</td>
<td>1958–1961</td>
<td>Yes</td>
<td>M 26.0/F 29.4*</td>
<td>M 72.8/F 80.2*</td>
<td>M 2.8/F 2.7*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1959–1960</td>
<td></td>
<td>M 29.9/F 36.5++</td>
<td>M 81.9/F 93.0H++</td>
<td>M 2.7/F 2.5++</td>
</tr>
<tr>
<td>Babigian, 1975 (90)</td>
<td>First admission rate Monroe County, New York State</td>
<td>1970</td>
<td>Yes</td>
<td>M 38/F 28</td>
<td>M 56/F 67</td>
<td>1.5/F 2.4</td>
</tr>
<tr>
<td></td>
<td>First contact rate</td>
<td></td>
<td></td>
<td>M 74/F 53</td>
<td>M 144/F 137</td>
<td>M 1.9/F 2.6</td>
</tr>
</tbody>
</table>

† Anglo-Americans.
‡ Native white subjects.
§ Native non-white subjects.
¶ Born in Ohio.
** Born in other States.

black persons, 274 and 263 per 100 000, while they markedly decreased in white persons, from 61 to 32 per 100 000. In Tennessee (94), black patients represented 48% of in-patients admissions (involuntary) and 37% of out-patients but only 16% of the state population. In Indiana (95), black persons represented 7% of the total population but the proportion of black patients admitted for schizophrenia was much higher, ranging between 28% in 1988 and 33% in 1995: black subjects were four times more likely than white subjects to be diagnosed with schizophrenia. Differential admission of black patients to public hospitals can only explain a small proportion of this astonishing difference.

Two prospective studies have confirmed a relationship between black ethnicity and schizophrenia. The National Collaborative Perinatal Project (96) found that African American ethnicity was associated with a two-fold increased risk of adult schizophrenia. An incidence study in Alameda County (97) observed that African Americans were approximately three times more likely than white persons to be diagnosed with schizophrenia. After adjusting for socioeconomic status indicators at birth, the risk was still about two-fold. The risk was specific for schizophrenia and was not observed for other schizophrenic disorders. It is worth underlining that the sample was constituted by an urban, fully insured population; consequently the results were not influenced by ‘gross disparities in health care access and socioeconomic circumstances in family of origin’ or by the rural/urban factor.

Discussion

Validity of the results

This review compares studies in countries of recent and longstanding immigration conducted with dissimilar methodologies reflecting the different decades in which they were performed. Studies in countries of recent immigration were first contact studies, used the most recent criteria, and were performed in the last 30 years. By contrast, studies in countries of longstanding immigration relied on hospital admission data, used outdated criteria for diagnosing schizophrenia, and were performed up to 80 years ago. However, as previously
The increased risk for schizophrenia continues to be observed in the second generation of immigrants to European countries, even when considering only the non-black immigrants (67, 68, 101, 102). The few studies on this issue in countries of longstanding immigration also observed an increased risk in the second generation. In Israel (73), the hazard ratios were similarly augmented in the first and second generation immigrants. In the white population of New York State for 1929–1931 (21) and 1949–1951 (22, 75) the rate for the offspring of foreign-born persons was intermediate between that of foreign-born persons and of the offspring of native-born persons. In this population, as previously noted, the risk ratio between foreign-born and native subjects decreased progressively from 1.5 in the 1930s to 1.1 in the 1960s (21, 75, 76), in line with a mounting proportion of second generation immigrants among the native-born population. No later data for New York State are available. It is quite possible that the rates for the native population continued to increase, as it would be comprised of more and more descendants of immigrants; it might even surpass the rates of foreign-born subjects, as the offspring of immigrants were exposed either longer than new immigrants or at a more vulnerable period. This could explain the paradoxical results of lower rates for all admissions for schizophrenia in recent immigrants reported by Morgan and Andrushko in Toronto (103).

If these conclusions of an increased risk for schizophrenia in countries of longstanding immigration are correct, they suggest that there is a hidden epidemic of schizophrenia in the immigrant populations in North America. The lack of data on this issue in the last decades does not allow verification of this assertion, but it is possible to infer some support from recent Canadian and US data.

A comparative study (99) of five major psychiatric centers in the US and one in Toronto found that the proportion of schizophrenia cases did not decline between 1972 and 1988 in the Canadian hospital, contrary to the US ones. In fact the number of its beds dedicated to patients with schizophrenia increased by 11%. It is quite possible that this increase is related to the large proportion of first and second generation immigrants in Toronto, who together represent 76% of the adult population (51). In British Columbia, Goldner et al. (104) used administrative data for the 2.7 million adult residents and found average 1 year prevalence rates of 4.5, 4.5 and 4.2 per 1000 for 1996–1997, 1997–1998, 1998–1999; these figures are in the medium range when compared
with the international data (4). The rates in the city of Vancouver were moderately increased, which is consistent with an urban effect. But in one district of Vancouver, the rates were three to four times higher for the three study periods being 18.5, 15.7 and 16.2 per 1000 respectively. The proportions of first and second generation immigrants were not available separately by district, so it is not possible to test the hypothesis that they were correlated with the schizophrenia rates. In the same province, Bray et al. (105) followed a cohort of subjects born between 1975 and 1985. She found an increase in schizophrenia rates between 1989 and 1998 from 66.6 to 119.6 per 100 000 in males and from 77.1 to 89.9 per 100 000 in females. The observed increase cannot be related to the proportion of foreign-born subjects (1.3% in this cohort) or to that of black subjects (<1.0% in this province). It could be related to the proportion of second generation immigrants included in the cohort, which is not given in the study. For comparison, data from Finland (106), one of the countries with the highest incidence in cohort studies, showed that the incidence of schizophrenia in cohorts born between 1954 and 1965 declined from 79 to 53 per 100 000 in males and 58 to 41 per 100 000 in females, although the subjects were followed to a later age than for Bray et al.

A US cohort study in Alameda County (107) also found high incidence rates of schizophrenia, which could only partly be accounted for by the increased rates in black subjects. The Epidemiological Catchment Area study (92) found high prevalence rates of schizophrenia in the US compared with the median of international studies: 9 per 1000 for 1 year prevalence and 13 per 1000 for lifetime prevalence. Given the importance of Hispanic immigrants to the US, it is surprising to find so few data regarding schizophrenia rates in this group. Recent epidemiological studies in Hispanic populations did not include psychotic disorders. An early study by Malzberg (108) found that Puerto Ricans recently arrived in the US were 1.8 times more at risk to be admitted for schizophrenia compared with the remaining population of New York State. The results concerning psychotic disorders in the study by Shrout et al. (109) were difficult to assess because of the small sample sizes of the Mexican American immigrant and native groups, as well as differences in interpreting symptoms. Self-reported psychotic symptoms were more frequent among the second than the first generation of Mexican immigrants, 26.9% vs. 12.4% (110). In a very large sample of veterans with psychoses (111), Hispanic patients were 2.9 times more likely than white ones to be diagnosed with schizophrenia.

To summarize, there is an urgent need in North America for data on the relationship between immigrant status and schizophrenia and its related disorders. Because of the low incidence of psychotic disorders, epidemiological studies have to be specifically designed to examine this relationship, as was the AESOP study in the UK (8, 102).

More elevated risk for schizophrenia in dark skinned subjects. This review observes that black immigrants to Canada and Israel have a higher risk for schizophrenia than do other immigrants. This finding is similar to European results although both the immigrants and the host countries differ markedly. African subjects living in Africa have prevalence rates comparable to those observed for native-born populations in most countries. Subjects of African ancestry living in the Caribbean do not have an increased risk compared with the native populations in the UK or the Netherlands. The situation is quite different in African Americans living in the US for whom this review indicates the existence of an unrecognized epidemic, as their risk for schizophrenia is at least twice that of the white population. These results are remarkable as African Caribbeans and African Americans share common lineage and abduction from Africa. It means either that African Americans living in the US are exposed to a risk factor or that African Caribbeans are exposed to a protective factor.

It is hypothesized that vitamin D is both the risk factor when deficient or insufficient and the protective factor when at normal levels. The precise range of levels that are normal remains to be determined (112, 113). Gupta (42) was the first to suggest that the elevated rates of schizophrenia, diabetes mellitus and multiple sclerosis in immigrants, as well as autism in their children, may be related to a single environmental agent. McGrath (114) was the first to propose that prenatal vitamin D deficiency may contribute to schizophrenia. An initial study (115) found a trend in black subjects between maternal circulating vitamin D levels during the first trimester of pregnancy and schizophrenia in the offspring. A second study (116) observed a remarkable protective effect of vitamin D supplementation during the first year of life in males, but it was not possible to calculate the risk for females. As the neuroprotective functions of vitamin D began to be better recognized (117–119), prenatal (120–122) or both prenatal and adult (123) deficiency or insufficiency of this vitamin has been proposed as a risk factor for schizophrenia.
As most authors now consider schizophrenia to be a neurodevelopmental disorder, the similarities in the epidemiology of schizophrenia and that of autism regarding immigrant status and skin color are striking. The rates of autism are very elevated in children of immigrants compared with those of native populations, and especially in children of dark skinned immigrant mothers (9–18). In children of black mothers in the US the risks are augmented, but less so (124, 125). Extremely low numbers of autism were reported by the first study on autism in Africa (126) and the figures were still lower in African children of African parents who had not left Africa.

It is hypothesized that, when occurring prenatally, vitamin D deficiency or insufficiency is involved in the genesis of autism (127) and schizophrenia (114) and that, when occurring later in life, it is involved in the genesis of adolescent, adult or late-onset schizophrenia (123). Prenatal deficiency would be associated with more cognitive as well as negative symptoms and poorer outcome, later deficiency with more positive symptoms and better outcome. The vitamin D hypothesis is consistent with the extreme rarity of schizophrenia in rural societies and its rapid rise with industrialization (128), when more people were working indoors and so were less exposed to sunlight with consequent decreased vitamin D levels. It is also consistent with the observations that schizophrenia was virtually unknown in Africa before the white colonization and that in so-called primitive society’s persons developed the disease soon after they were exposed to the Western way of life (129). This way of life includes Western-style clothing and living indoors, both of which decrease sun exposure and consequently decrease vitamin D levels. It is also consistent with the observation that in Africa, contrary to what is observed in the Western world, schizophrenia rates are positively associated with education level (130, 131). The observation that some persons developed schizophrenia rapidly after a sustained decrease in sun exposure (129) suggests the existence of an individual vulnerability to the brain effects of vitamin D insufficiency. It also suggests that the required serum level for optimum brain functioning remains to be determined.

The vitamin D hypothesis would also explain the better outcome observed in developing countries by early studies (132), as patients who were not affected by prenatal vitamin D deficiency developed the disease after an abrupt decrease in vitamin D levels later in life. It would also explain why this better outcome is not observed today (133), as more subjects in the developing countries are affected by prenatal vitamin D deficiency. The vitamin D hypothesis would be consistent with the higher risk for tardive dyskinesia observed in non-white subjects (134), as this could be attributed to more neurological damage due to a more severe prenatal vitamin D deficiency. This is similar to the observation that autism in children of black mothers is more often associated with mental retardation (Dealberto, submitted), likely due to a more severe prenatal vitamin D deficiency.

The hypothesized effect of vitamin D insufficiency is probably of great magnitude, and may overwhelm the epidemiology of schizophrenia. It would explain several known factors in the epidemiology of schizophrenia, especially the association with urban birth and urban living, winter birth, the rural/urban differences and the augmenting rates with higher latitudes. If the vitamin D hypothesis is proven, the increased risk for schizophrenia observed in black subjects would be related to skin color and not to ethnic origin, although these are correlated (135).

Increased risk for psychosis in all immigrants. The vitamin D hypothesis does not, however, explain the overall increased risk for schizophrenia in immigrants whatever their skin color. Both black and non-black immigrants have a higher risk than do native-born subjects for schizophrenia (2), manic, depressive and other psychoses (8) and affective psychoses (73, 102). The second generation remains at higher risk (67, 73, 101, 102). This increased risk is linked to immigrant status independent of skin color. Malzberg (77) reported an increased risk for both schizophrenia and manic depressive psychoses in black immigrants compared with black subjects living in the US. In contrast African Americans long established in the US do not have an increased risk for bipolar disorders. The study by Barnes in Indiana (95) is especially striking: from 1988 to 1995, the proportion of black subjects admitted for mood disorders varied yearly around 7%, which was the proportion of the black population in this state.

Consequently it appears that another mechanism, independent of skin color, is involved in the increased risk for schizophrenia and other psychotic disorders observed across all immigrants. Any postulated mechanism should affect the immigrants throughout their life in the host country. It should be transmissible to the second generation. It should not to be related to racism, as it is observed in immigrants to different countries with different cultures. The role of
socioeconomic conditions is uncertain, as two studies have reported that they were superior in immigrants than in native-born population (77, 136). The Taiwanese study (136) is particularly interesting as it compared Chinese immigration before 1895 and after 1945; although recent immigrants had better education and superior positions than descendants of previous immigrants, they had a higher prevalence of schizophrenia, with a ratio equal to 1.8.

This review proposes a second hypothesis. It is that epigenetic mechanisms activated by a yet unknown trigger (stress, change in diet, or other) are involved in the genesis of psychotic episodes observed in schizophrenia and other psychoses. Epigenetics refer to modifications in gene expression controlled by heritable but potentially reversible changes in DNA methylation and/or chromatin structure (137). The heritability would explain why the second generation of immigrants is affected. Epigenetics have previously been proposed as causal mechanisms for schizophrenia (123, 138–140), but the epidemiological findings suggest that they are also involved in other psychoses.

According to the principle of parsimony, it is unusual to propose two hypotheses for a single disorder. However schizophrenia is a very complex disease and to postulate its phenomenology ranging between a pole of neurodevelopmental disorders and a pole of psychotic disorders is consistent with its many diverse clinical presentations.

Acknowledgements

I remain indebted to my foreign-born patients who compelled me to acknowledge the existence of an increased risk for schizophrenia and psychosis in immigrants.

References

Immigration, ethnicity and schizophrenia


67. Veling W, Selten JP, Veen N, Laan W, Blom JD, Hoek HW. Incidence of schizophrenia among ethnic minorities in the
86. Lazarus J, Locke BZ, Thomas DS. Migration differentials in mental disease: state patterns of first admissions to mental hospitals for all disorders and for schizophrenia, New York, Ohio and California, as of 1950. Milbank Mem Fund Q 1963;41:25–42.
schizophrenia in the prenatal determinants of schizophrenia study. Schizophr Bull 2000;26:297–308.


112. Vieth R. What is the optimal vitamin D status for health? Progr Biophys Mol Biology 2006;92:26–32.


