

Schizophrenia among ethnic minorities

Social and cultural explanations for the increased incidence of schizophrenia among first- and second-generation immigrants in the Netherlands

Willem Anne Veling

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Schizophrenia among Ethnic Minorities

Social and cultural explanations for the increased incidence of schizophrenia among first- and second-generation immigrants in the Netherlands

Schizofrenie bij etnische minderheden

Sociale en culturele verklaringen voor de verhoogde incidentie van schizofrenie bij eerste- en tweede-generatie immigranten in Nederland

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Summary

Differences in health have been documented among ethnic groups in many countries. The incidence of schizophrenia and other psychotic disorders is high among ethnic minority groups in several countries in Western Europe. In the Netherlands, immigrants from Morocco, Surinam, and the Netherlands Antilles have an increased risk of schizophrenia compared to the majority population. As yet these findings have defied explanation. High incidence rates in the countries of origin, selective migration, diagnostic bias, or variation in the frequency of putative risk factors such as obstetric complications or exposure to viruses, do not account for the immigrants' elevated risk. Increasingly, researchers suspect that adverse social experiences of immigrant groups are an explanation. Socioeconomic disadvantage, long-term separation from parents during childhood, ethnic density, social disorganization of the neighborhood, racial or ethnic discrimination, acculturation strategies, and weak ethnic identity have been suggested as factors that may contribute to the increased incidence, but only few studies have evaluated some of these hypotheses.

This thesis provides more insight into the increased incidence of schizophrenia among first- and second-generation immigrants, by investigating the social context of schizophrenia among immigrants both at the individual level and at the group level, and by studying aspects of acculturation as potential determinants of schizophrenia.

In chapter 2 we describe incidence rates of schizophrenia in ethnic groups. A first-contact incidence study of psychotic disorders in The Hague showed that the risk for schizophrenic disorders was increased for first- and second-generation immigrants from Morocco, Surinam, and Other non-Western countries. The risk was particularly high for second-generation immigrants and for Moroccan males, and was relatively low for Turkish immigrants.

Chapter 3 reports ethnic differences in symptoms at the time of first treatment contact. Immigrants from Morocco not only had the highest risk of schizophrenia, Moroccan patients also had more severe symptoms than native Dutch patients, and presented more often with persecutory delusions, bizarre behavior and visual hallucinations. Moroccan and Turkish patients more often met the criteria for a current depressive episode.

Chapters 4 and 5 show the influence of two aspects of the social context on the incidence of psychotic disorders.

First, the neighborhood context was strongly associated with the risk of psychotic disorders among immigrants from Morocco, Surinam and Turkey (Chapter 4). Compared to native Dutch, the incidence was increased most significantly among immigrants living in neighborhoods where their own ethnic group comprised a small proportion of the

population. In low ethnic density neighborhoods, immigrants had a markedly increased risk, whereas in high ethnic density neighborhoods, the incidence rate was not significantly higher than that of native Dutch.

Second, the incidence varied among ethnic minority groups according to degree of perceived discrimination (Chapter 5). Based on a population study and on rates of reported incidents of discrimination in The Hague, the degree of perceived discrimination of ethnic minority groups was rated: high (Morocco), medium (Netherlands-Antilles, Surinam and Other non-Western countries), low (Turkey), or very low (“Western or westernized countries”). The incidence of psychotic disorders was higher in groups which reported more discrimination, independent of neighborhood socioeconomic deprivation.

Next, the role of social and cultural factors as potential risk factors for schizophrenia is described. A matched case-control study of first-episode schizophrenia in non-Western ethnic minority groups investigated whether aspects of acculturation were associated with schizophrenia. Individuals who had developed schizophrenia reported somewhat higher rates of perceived discrimination in the year prior to illness onset than their siblings and matched general-hospital controls, but these differences were not statistically significant (Chapter 6).

Weak and negative identification with one’s own ethnic group was a strong determinant of schizophrenia (Chapter 7). Individuals who developed schizophrenia identified themselves less often and less positively in the year before illness onset with their own ethnic group than controls. A separated identity, defined as positive identification with the own ethnic group but not with the Dutch majority group, was associated with a lower risk of schizophrenia.

Chapter 8 explores associations between cannabis, genetic predisposition for schizophrenia, and ethnicity. Cases had used cannabis approximately three times more often than their siblings and matched general-hospital controls. Siblings of schizophrenia patients had not used cannabis more often than general hospital controls, in spite of their higher genetic predisposition for schizophrenia. Turkish participants had used cannabis less often than those from other ethnic groups, but the relationship between cannabis and schizophrenia was similar within each ethnic group.

In the final chapter, we summarize the main findings of the thesis. These results suggest that the increased incidence of schizophrenia and other psychotic disorders among first- and second-generation immigrants can be understood by the social and cultural context in which immigrants live. The increased incidence is likely to be determined

by factors on multiple levels, including the neighborhood, the ethnic group, and the individual. Specifically, the risk of psychotic disorders increased by belonging to a group that experiences a high degree of discrimination, and by having a weak and negative identification with one's own ethnic group. These factors may represent a situation of chronic social stress, which might precipitate schizophrenia in individuals who have a (genetic) predisposition for the illness. Cannabis use was an independent risk factor for schizophrenia. It was not correlated with genetic predisposition for the illness, but was associated with perceived discrimination and a negative ethnic identity, suggesting that cannabis use may be a consequence of social stress.

Living in a neighborhood with many other members of one's own ethnic group was associated with a lower risk of schizophrenia, as was having a strong and predominant orientation towards one's own ethnic group (a separated identity). These factors may buffer or prevent social stress. In the face of discrimination and social adversity, it may be essential for first- and second-generation immigrants to retain a positive identification with their own ethnic group and to seek positive distinctiveness from the majority group.

The findings have several implications. The results of this thesis make clear that the social context matters in the etiology of schizophrenia. Further research in this area should incorporate both individual factors and contextual factors. More research is needed to understand the relationship between perceived discrimination and schizophrenia, and to investigate ethnic identity and other aspects of social identity as risk factors for schizophrenia. Prospective studies are needed to disentangle cause and effect. For instance, ethnic identity may be measured in individuals with a high risk for schizophrenia, to investigate whether transition to psychosis is predicted by weak and negative ethnic identity. The influence of protective factors such as high ethnic density and social capital on the incidence of schizophrenia could be further studied. If social and cultural factors may indeed prove to be causally related to schizophrenia, treatment could focus on influencing these factors, and preventive strategies might be developed. Several suggestions for treatment and prevention are given.

1

Introduction

Ethnic inequalities in health

Differences in health, in terms of both morbidity and mortality, have been documented time and again among ethnic groups in many countries¹⁻³. In the Netherlands, a growing body of data indicates that ethnic minorities experience poorer general health than the majority population, and have more chronic health problems⁴⁻⁶. For instance, the prevalence of diabetes among Surinamese, Moroccan and Turkish immigrants is three to six times higher than in the majority population⁷; Surinamese immigrants have higher rates of hypertension⁶; and immigrants from Morocco and Turkey make contact with health care services more frequently for digestive problems, stomach ulcers and low back pain^{8,9}. On the other hand, mortality rates among most non-Western immigrant groups in the Netherlands are similar to those of native Dutch people¹⁰.

With regard to mental health, patterns of psychiatric diagnoses among ethnic groups vary. Some studies found elevated rates of psychiatric morbidity among immigrants^{11,12}. In particular, the incidence of schizophrenia and other psychotic disorders has been reported to be higher in several ethnic minority groups in the United Kingdom and Scandinavia¹³. The prevalence rate of non-psychotic psychiatric disorders, however, was similar or lower in most ethnic minority groups compared to the white populations in the United States and the United Kingdom¹⁴⁻¹⁶. In the Netherlands, there is no clear picture of mental health differences among ethnic groups. Increased rates of schizophrenia have been found among Surinamese, Antillean and Moroccan immigrants¹⁷, a pattern consistent with the international literature. In addition, there is some evidence that Turkish immigrants have increased rates of minor psychiatric disorders¹⁸ and emotional problems¹⁹; older Moroccan and Turkish immigrants reported more depressive symptoms than native Dutch people²⁰, and Antillean, Surinamese and Moroccan immigrants may have a higher risk of developing drug use disorders²¹. Other studies, however, have not found substantial mental health problem differences between ethnic minorities and native Dutch^{6,22}.

It is clear that more research is needed to investigate ethnic inequalities in (mental) health, not only to obtain more reliable data of the distribution of illness across social groups, but also, and more importantly, to advance our understanding of the mechanisms underlying health inequalities and our search for the causes of disorders. Given the heterogeneity of the findings to date, research should clearly differentiate specific ethnic groups as well as specific health outcomes. This thesis focuses on differences in the incidence of schizophrenia among ethnic groups, which have been consistently reported, but have as yet defied explanation^{13,23}.

Characteristics of immigrant groups in the Netherlands

In this thesis we use the classification of ethnicity as defined by the Netherlands' Bureau of Statistics ²⁴. Dutch ethnicity is assigned to citizens who are Dutch-born and whose parents were also born in the Netherlands (hereafter referred to as native Dutch). If a citizen was born abroad, he or she is considered a first-generation immigrant, and is assigned to the group of people born in the same country. A Dutch-born citizen is considered a second-generation immigrant if at least one parent was born abroad. If the parents were born in different foreign countries, the country of birth of the mother determines the assignment to a particular group. On January 1, 2005, the city of The Hague had 472,087 inhabitants, of whom 34.5% was a first or second-generation immigrant from any non-Western country. The three largest groups of first- and second-generation non-Western immigrants in The Hague were Surinamese (45,388), Turks (32,228) and Moroccans (24,144).

Labor migration from Morocco to the Netherlands began in the 1960s, predominantly from the Berber peoples living in the poor and rural Rif mountains in the north of the country. Many Moroccan men eventually brought their families and settled in the Netherlands, predominantly in the larger cities, including The Hague. The socioeconomic status of first- and second-generation Moroccan immigrants is generally poor compared to that of native Dutch: their level of education is lower; they are more often unemployed, and live more often in disadvantaged neighborhoods and on minimum incomes ²⁵. Nearly all Moroccans identify themselves as Islamic ²⁵. Studies indicate that of all ethnic minorities, Moroccan immigrants are disliked most by the native Dutch population ²⁵. They are lowest in the ethnic hierarchy ²⁶ and report the highest degree of discrimination ²⁷.

The Dutch colony of Surinam, bordering the Caribbean region, gained independence in 1975. Doubts about its future caused mass emigration to the Netherlands during the period 1971-1981. The Surinamese population is ethnically diverse. In The Hague the majority is East-Indian, with Hindu or Islamic religion. Their ancestors migrated in the 19th century from British India to Surinam. A minority of the Surinamese is of African origin. Because Surinam is a former colony, nearly all immigrants speak Dutch fluently.

Turkey is an Islamic country, with a secular administration oriented towards Europe. In 1964 the Dutch government signed an agreement with Turkey to recruit migrant labor ("guest workers"). Uneducated young men came, mainly from poor rural areas in middle and eastern Turkey. Many of these men decided to stay in the Netherlands and to bring their families after a few years. Today the number of Turkish immigrants is still increasing because of marital migration. Their socioeconomic position is similar to that of Moroc-

can immigrants²⁵. Among immigrants in the Netherlands, first- and second-generation Turks identify most strongly with their own group²⁵. They report a low degree of discrimination²⁷, although this has increased since the terrorist attacks of 9/11²⁵.

Immigration from western countries started in the 1960s as well, when guest workers from southern Europe (Spain, Italy, Greece) were recruited. Another large western immigrant group is that of refugees from former Yugoslavia, who came to the Netherlands in the 1990s. A third group of western immigrants consists of citizens of the European Union, which established a free labor market for its citizens in 1993.

The group of other non-Western immigrants includes immigrants from the Netherlands Antilles, former Dutch colonies in the Caribbean. They move to the Netherlands mainly for reasons of study and work. Like many Caribbean islands, the society of the Antilles has its origins in plantation slavery. The population is ethnically diverse, with a black (African) majority, and smaller white and mixed groups. Although Dutch is the official language, Papiamentu, the local language, is spoken in most households. Other non-Western immigrants to the Netherlands are mainly refugees from African and Asian countries, who arrived in the 1980s and 1990s.

Schizophrenia

Clinical description

Schizophrenia is a major mental disorder, ranked by the World Health Organization (WHO) as one of the world's top ten causes of long-term disability²⁸. It is a clinical syndrome that becomes manifest in adolescence or early adulthood, with severe and long-lasting effects on mental and physical health, and on psychosocial functioning²⁹. Schizophrenia is characterized by psychotic symptoms, 'negative' symptoms and cognitive impairment³⁰. Psychotic symptoms involve hallucinations, that is, perceptual experiences not shared by others; delusions, defined as false personal beliefs that are not subject to reason or contradictory evidence and cannot be explained by a person's usual cultural and religious concepts; and formal thought disorder, with loss of associations between thought processes, resulting in illogical or incoherent reasoning and speech. Negative symptoms are deficit states in which basic emotional and behavioral processes are diminished or absent. These symptoms include anhedonia (lack of pleasure), apathy (diminished ability to initiate and follow through on plans), alogia (reduced quantity or content of speech) and affective flattening (immobile facial expression, monotonous voice tone)³⁰. Cognitive impairment includes problems in attention and concentration, psychomotor speed, learning and memory, and executive functions³⁰. Frequently pa-

Table 1.1 Diagnostic criteria of schizophrenia

A Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

- delusions
- hallucinations
- disorganized speech (e.g., frequent derailment or incoherence)
- grossly disorganized or catatonic behavior
- negative symptoms, i.e., affective flattening, alogia or avolition

B Social/occupational dysfunction: For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic or occupational achievement).

C Duration: Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D Schizoaffective and Mood Disorder exclusion: Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E Substance/general medical condition exclusion: The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Source: DSM IV³²

tients fail to appreciate that their symptoms are caused by illness²⁹. As a result of these symptoms, many patients lose their capacities to keep a job, to maintain relationships with partners and friends, to take care of themselves and their loved ones.

There are no sensitive or specific neurobiological markers of schizophrenia³¹. The diagnosis of schizophrenia is based on internationally accepted criteria that describe and define the symptoms of the disease. Table 1.1 shows the diagnostic criteria according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV)³².

The symptoms and the course of schizophrenia differ among individuals, but typically, there is a prodromal period preceding the onset of psychotic symptoms, with subtle thought, language, perception or mood disturbances and problems in maintaining or initiating social contacts³³. After onset, psychotic symptoms fluctuate over time, but 70-80% of the patients treated for a first episode of schizophrenia have a relapse of psychotic symptoms within five years²⁹. Negative symptoms and cognitive impairments are more stable, and are important determinants of psychosocial functioning. The illness process usually plateaus within five to ten years after onset, and does not manifest further deterioration throughout the life course³⁴.

Etiology

The causes of schizophrenia remain largely unknown, but include genetic and nongenetic factors³⁵. Data collected from families, twins and adoptees have shown that there is a large genetic component in liability to schizophrenia³⁶. The lifetime risk of schizophrenia in the general population is about one percent, but approximately ten times higher in the siblings or offspring of patients with schizophrenia; the concordance for schizophrenia in monozygotic twins is 50%³⁶. To date, it is unclear which genes contribute to schizophrenia, but linkage and association studies have suggested several candidate genes, including DTNBP1, NRG1, G72, RGS4, COMT and TRAR4³⁷. A meta-analysis of twin studies estimated that the heritability of liability to schizophrenia is approximately 80%, and found evidence that ~11% of schizophrenia liability resulted from shared environmental risk factors³⁸. These findings indicate that "liability to schizophrenia is largely genetically *mediated*, but not genetically *determined*, and thus is a *complex* trait, determined by genes, environment, and their interaction"³⁷.

Many different environmental risk factors and antecedents have been studied. Prenatal and perinatal events have been associated with development of schizophrenia later in life, including severe malnutrition during pregnancy³⁹, prenatal infections⁴⁰, obstetric complications⁴¹, high paternal age⁴², and winter birth⁴³.

Several social and sociodemographic factors have been associated with increased risk of schizophrenia. Poverty and lower socioeconomic status have long been linked to higher rates of schizophrenia⁴⁴⁻⁴⁶, but results were variable and generally modest^{29,47,48}, and it has proven to be difficult to establish the direction of the association, as lower socioeconomic status may both be cause and consequence of schizophrenia^{44,49}. Recently, cannabis use has been reported to be related to an increased risk of schizophrenia⁵⁰. A meta-analysis of all published prospective studies calculated a twofold risk of schizophrenia for those exposed to cannabis during adolescence⁵¹. Part of this association may be explained by genotype-environment interaction (schizophrenia genes controlling sensitivity to cannabis psychotogenic effects)⁵², and part by genotype-environment correlation (schizophrenia genes controlling likelihood of cannabis use)⁵¹, but the possibility of genotype-environment correlation has not yet been explored. Other sociodemographic risk factors are urban birth and upbringing^{43,53}, single marital status⁵⁴, and, as mentioned earlier, migrant status¹³.

Incidence

In the 1980's, the WHO initiated the landmark Ten Country Study^{55,56}, in order to investigate with uniform methodology the incidence of schizophrenia in different countries around the world (including one developing country, India). The annual incidence of 'narrowly defined' schizophrenia ranged from 7 to 14 per 100,000, which led the

researchers to conclude that “The results provide strong support for the notion that schizophrenic illnesses occur with comparable frequency in different populations.”⁵⁵ This study has had strong influence on schizophrenia research, and has contributed to a widespread belief that the incidence of schizophrenia is uniform across space and time⁵⁷. It is questionable whether such conclusions are justified. The results of the Ten Country Study itself showed that the incidence rate of narrowly defined schizophrenia in the site with the highest incidence actually was two times as high as that of the site with the lowest incidence. When in the same study the researchers used a wider definition of schizophrenia, one that resembles the DSM and ICD classifications of schizophrenia, the incidence of schizophrenia varied from 16 per 100,000 in Honolulu, USA, to 42 in rural Chandigarh, India⁵⁶. More recently, a systematic review including 158 incidence studies found a median incidence rate of 15.2 per 100,000 person-years, and the 10% and 90% quantiles ranged from 7.7 to 43.0 per 100,000, which is a 5.6-fold difference⁵⁸.

In the Netherlands, a study participating in the WHO Collaborative Study on the Assessment and Reduction of Psychiatric Disability found in the provinces of Groningen and Drenthe an administrative incidence rate for functional nonaffective psychosis of 11.2 per 100,000⁴⁸. More recently, Selten and colleagues reported a first-contact incidence rate in The Hague of 21 per 100,000 for schizophrenia and 35 per 100,000 for any psychotic disorder¹⁷.

Incidence of schizophrenia among immigrants

As indicated earlier, the incidence of schizophrenia is higher in several immigrant groups throughout the world. In the early 1930s, Ødegaard found that Norwegian immigrants in the USA were admitted to a psychiatric hospital for schizophrenia twice as often as native-born Americans or Norwegians in Norway⁵⁹. Two decades later, Malzberg described higher first-admission rates for schizophrenia among the foreign-born residents of New York State, independent of differing population age structures and degree of urbanisation⁶⁰. Subsequently, in the 1960s, studies in the United Kingdom found that African-Caribbean immigrants had higher rates of schizophrenia than the native British population^{61,62}. These findings were controversial, because the early studies had substantial methodological problems, including inadequate (immigrant) population denominator data, use of non-standardized diagnoses and uncertainty with regard to the completeness of case ascertainment⁶³. Later studies used prospective case finding within defined catchment areas, standardized assessments and diagnostic criteria of psychopathology, and more accurate census data. Even then higher rates of schizophrenia were found in African-Caribbean immigrants^{64,65}, as well as in other ethnic minority

groups in the United Kingdom⁶⁶. Recently, a large three-center incidence study (the AESOP study, conducted in London, Nottingham and Bristol) found strikingly increased rates of schizophrenia in African-Caribbeans (Incidence Rate Ratio [IRR] = 9.1 [95% CI, 6.6-12.6]) and Black Africans (IRR = 5.8 [3.9-8.4]) compared to the white British population, and modestly increased rates in Asian and other immigrants⁶⁷. In this study, a substantial part of the immigrant groups consisted of second-generation immigrants. Interest in the relationship between migration and schizophrenia is not limited to the USA and the UK. Several studies in Sweden and Denmark also found high incidence rates of schizophrenia among immigrants⁶⁸⁻⁷¹. In the Netherlands, there are fewer studies on the incidence of schizophrenia among immigrants. In 1994 and 1997, Selten and colleagues studied national hospital register data, and reported significantly higher first-admission rates for schizophrenia in male and female immigrants from Surinam and the Netherlands Antilles, and in male immigrants from Morocco^{72,73}. In a two-year first-contact incidence study in The Hague, the risk of schizophrenia was significantly increased for Surinamese (age- and gender-adjusted IRR = 3.7 [95% CI, 2.2-6.1]) and Moroccan (adjusted IRR = 5.0 [95% CI, 2.8-8.9]) immigrants, but not for Antillean (IRR = 2.2 [0.7-7.2]) and Turkish immigrants (IRR = 0.6 [0.2-2.1])¹⁷. The power of the study prevented a reliable analysis of first- and second-generation immigrants separately, but preliminary results suggested that the risk was higher for those of the second-generation. In 2005, a meta-analysis that included the results of 18 incidence studies was published¹³. The mean weighted relative risk for developing schizophrenia among first-generation migrants (40 effect sizes) was 2.7 (95% CI, 2.3-3.2). The risk for second-generation migrants (only seven effect sizes) was 4.5 (95% CI, 1.5-13.1)¹³.

Possible explanations for the increased incidence among immigrants

Increased risk in country of origin

Given the range of incidence rates around the world, the most straightforward explanation would be that the incidence is higher in the countries of origin.

Several incidence studies have been undertaken in countries where immigrants with increased risks come from, especially in the Caribbean region⁷⁴⁻⁷⁶. One of these studies was conducted in Surinam⁷⁷. We are not aware of any published incidence studies in Morocco or Turkey. In the studies, incidence rates in the countries of origin were lower than those reported for immigrants to western Europe, and within the reported range for other populations worldwide.

Diagnostic bias

Western psychiatrists may more readily assign severe diagnoses such as schizophrenia to immigrant than to non-immigrant patients. Also, psychotic symptoms may be misinterpreted by clinicians and researchers who are not familiar with the culture of immigrant patients. Content and severity of psychotic symptoms may be influenced by cultural background⁷⁸⁻⁸⁰. Several studies in the USA and the United Kingdom investigated symptom profiles in patients from different ethnic groups diagnosed with schizophrenia. Some studies did not find large differences across ethnic groups^{81,82}, while other studies suggested that hallucinations, paranoid and religious delusions, as well as manic symptoms may be reported more often or may be more severe among patients from certain ethnic minority groups^{79,83-86}.

The possibility of diagnostic bias was supported by one study in London, where the agreement between a Jamaican psychiatrist and his British counterparts about which African and African-Caribbean patients had schizophrenia was poor⁸⁷. Several researchers in the United States, who found higher rates of diagnosed schizophrenic disorders among African Americans⁸⁸⁻⁹⁰, also argued that their own findings should be attributed to diagnostic bias. They predicted that differences in rates of schizophrenia would disappear with the use of (semi-) structured interviews and careful application of DSM criteria^{88,89,91,92}. However, recent work has shown that standardized assessments do not completely resolve these issues⁹³⁻⁹⁵.

Thus, although making a diagnosis of psychotic disorders among different ethnic groups is difficult, and diagnostic bias is a real possibility, a large and still increasing number of studies in different settings and countries indicates that significant ethnic differences in the incidence of schizophrenia remain, even when structured interviews, blinding for ethnicity, information from family members, and strict diagnostic criteria are used¹³.

Selective migration

Since the 1930s, selective migration of persons prone to the development of schizophrenia has been considered as a major explanation for the increased risks among immigrants⁵⁹. This hypothesis has been challenged by several findings. The fact that not less than one third of the total population of Surinam emigrated to the Netherlands after independence in 1975 makes selective migration highly unlikely⁹⁶. Moreover, individuals migrate for widely different reasons. In general, the healthy and physically most able are most likely to migrate. This is especially plausible for labor migrants, such as African-Caribbeans in the United Kingdom and Moroccans and Turks in the Netherlands, who migrated because of job opportunities.

Another argument against the hypothesis of selective migration is that it does not easily explain the higher risks among second-generation immigrants.

Established risk factors for schizophrenia

Although obstetric complications have been found to be associated with an increased risk of later schizophrenia^{41,97}, in the only study comparing ethnic groups, obstetric complications were almost twice as common in white as in African-Caribbean patients in the United Kingdom⁹⁸.

Several studies suggest that prenatal exposure to infections such as influenza, rubella, or toxoplasmosis is associated with adult schizophrenia^{40,99,100}. Immigrant women may have little immunity to certain microorganisms, or may have been exposed more often during pregnancy. To date no evidence has been found to support this hypothesis^{101,102}.

There is a growing consensus that cannabis use is a risk factor for schizophrenia^{103,104}. There is no evidence that the rate of cannabis use in first-episode ethnic minority patients is higher than that in patients from native populations in the United Kingdom or the Netherlands^{105,106}, but reliable population data on cannabis use in ethnic minorities in the Netherlands are lacking¹⁰⁷.

The social environment

Increasingly, researchers suspect that adverse social experiences of immigrant groups may contribute to their elevated risk of schizophrenia²³. We have made an overview of the literature with regard to the social factors that have been suggested as potential explanations, which is shown in Table 1.2 and will be discussed in the following paragraphs.

A case-control study of social environment, ethnicity and schizophrenia in the United Kingdom reported that a long period of separation from either or both parents as a

Table 1.2 Potential social risk factors or antecedents of schizophrenia among immigrants

	Related to	
	Incidence of schizophrenia / psychosis	Mental health of immigrants
Parental separation	+	+
Low socioeconomic status	++ / --	++
Neighborhood ethnic density	+	+
Social disorganization of the neighborhood	+	+
Discrimination	+	++
Acculturation strategies	?	++ / -
Weak ethnic identity	?	++

+ Some studies, evidence for an association.

++ More than five studies have reported an association.

- Some studies, but no evidence for an association.

-- More than five studies did not find an association.

? Has not been investigated.

child predicted schizophrenia in African-Caribbeans¹⁰⁸. This finding has recently been replicated in the AESOP study for immigrants and non-immigrants alike¹⁰⁹, and was interpreted to be an indicator of a range of early adverse social experiences, including family conflict and socioeconomic disadvantage.

Generally, immigrants have lower education, lower income and more often unskilled jobs than the non-immigrant population. A Swedish study found that poor socioeconomic status of the family household contributed to the higher hospital admission rates for schizophrenia among immigrants⁷¹, although differences remained significant after adjustment for socioeconomic status. Findings of clustering of new cases of schizophrenia in citizens born and raised in decaying inner-city areas^{46,110} have also renewed attention to socioeconomic disadvantage as risk factor for schizophrenia¹¹¹. This would hold especially true for immigrants, as they more often live in such deprived areas than do non-immigrants. However, it is unclear how low socioeconomic status or living in a disadvantaged neighborhood would lead to schizophrenia. Wicks suggested in her report on the association between childhood social adversity and the risk of developing psychosis later in life that "the social factors (single-parent household, parental unemployment, and receiving social welfare benefits) all represent a situation of exclusion. Maybe it is not the gradient of socioeconomic position but rather the adverse/excluding situations that influence the risk of developing schizophrenia and other psychoses"¹¹². This hypothesis connects to the seminal ecological work of Faris and Dunham in the 1930s in Chicago, who demonstrated that the hospital admission rates for schizophrenia were highest in areas characterized by social disorganization, and were increased among ethnic minorities who lived in neighborhoods with a low proportion of persons belonging to their own ethnic group⁴⁵. This field of research was rejuvenated by a study in London¹¹³, which reported a high incidence of schizophrenia for ethnic minorities who lived in neighborhoods with a low proportion of ethnic minorities. Recent results from the AESOP study suggested an association between ethnic fragmentation of neighborhoods and the incidence of schizophrenia¹¹⁴.

Faris and Dunham argued that ethnic minorities who live separated from other members of their ethnic group may find it difficult to develop and maintain positive affiliations with family members, neighbors and local institutions, thus increasing their sense of social isolation, which they hypothesized to be an important factor for the onset of mental disorders⁴⁵. Those ethnic minorities who live socially isolated may have an increased exposure to, and reduced protection against, stress and life events¹¹³.

Racial discrimination

A specific source of stress for ethnic minorities is racial/ethnic discrimination.

Many studies have shown that discrimination based on ethnic background, skin color or race (hereafter referred to as discrimination) has a pervasive, adverse influence on the

health of ethnic minority populations ¹¹⁵, but the relationship between discrimination and mental health is poorly understood ¹¹⁶, and research on the association between discrimination and psychosis is scarce ¹¹⁷. Some cross-sectional studies have reported an association between perceived discrimination and the prevalence of psychosis ^{118,119}, and a prospective study in the Netherlands suggested that perceived discrimination (albeit not only racial, but any discrimination) may induce the onset of delusional ideations ¹²⁰. The meta-analysis of incidence studies mentioned earlier found that the risk was particularly high for dark-skinned immigrants, who are likely to experience a higher degree of discrimination ¹³, but there has not been any research on the association between discrimination and the incidence of schizophrenia.

Acculturation and ethnic identity

In the context of investigating the social experiences of immigrants and their psychological adaptation in a society in which they constitute a minority of the population, the concept of acculturation has been developed. Redfield and colleagues defined it in 1936: "Acculturation comprehends those phenomena which result when groups of individuals having different cultures come into continuous first-hand contact, with subsequent changes in the original culture patterns of either or both groups."¹²¹ It is important to distinguish between group and individual levels of acculturation, because the phenomena at the two levels are different and may also have different consequences for mental health ¹²². Changes at the population level may occur in the attitudes of the majority population towards immigrant groups or in political organization, whereas changes at the individual level involve phenomena such as identity and values. Acculturation of ethnic minorities often brings positive changes in the socioeconomic position and in the physical and psychological well-being of groups and individuals, but can also be problematic. Berry introduced the notion of acculturative stress, to conceptualize the problems related to the process of acculturation ¹²³. It has been defined as "the response by individuals to life events that are rooted in intercultural contact, when they exceed the capacity of individuals to deal with them"¹²². Acculturative stress has been associated with mental health problems such as anxiety, psychosomatic symptoms and depressive symptoms ¹²⁴; the relationship with psychotic symptoms or schizophrenia has not been investigated.

The mental health consequences of acculturation depend to some extent upon what people try to do during their acculturation. Individuals have to make choices with regard to orientation towards their own ethnic group and orientation towards other groups. Based on these two dimensions, Berry distinguished four different acculturation strategies ¹²⁵. When individuals do not wish to maintain their cultural identity and seek daily interactions with other cultures, they are using the *assimilation* strategy. When they place a value on holding on to their original culture and at the same time wish to

avoid interacting with others, they are using the *separation* strategy. When people want to maintain their heritage culture and also have an interest in participating in other cultures, they choose the *integration* strategy. Finally, the *marginalization* strategy is used when there is little possibility or interest in cultural maintenance and little interest in having relationships with others ¹²⁵. It should be noted, however, that individuals may choose different acculturation strategies depending upon the situation of the moment: they may prefer the integration strategy at their workplace, while choosing the separation at home ¹²⁶. Also, ethnic minorities are not completely free to choose how they want to acculturate; integration, for instance, can only be achieved when the larger society accepts cultural diversity, and when there are positive mutual attitudes among minority and majority ethnic groups ¹²⁷. In the Netherlands, the official policy has been one of pluralism, of accepting cultural diversity, but recently, attitudes have changed towards greater insistence on adaptation to the Dutch culture ¹²⁸.

These distinctions notwithstanding, in general, the integration strategy has been associated with positive psychological adaptation and good mental health ¹²⁹, whereas marginalization has been shown to predict low self-esteem and poor mental health ^{125,130,131}. Some studies have found an association between assimilation and higher risk of psychological problems and mental disorders ^{124,132-134}; and some, but not all, studies reported lower rates of mental disorders among immigrants choosing separation ¹³⁴⁻¹³⁶. Most of these studies were cross-sectional, which means that the direction of the associations may also be reversed; for instance, poor mental health may lead to marginalization.

Closely related to the concept of acculturation strategies is *ethnic identity*, which can be thought of as one aspect of the acculturation process, as it focuses on subjective feelings about one's ethnicity ¹³⁰. Group identity among immigrants involves two distinct dimensions, similar to the dimensions of acculturation: ethnic identity, reflecting self-categorization as member of one's ethnic minority group and sense of belonging to this group, and national identity, considering and feeling oneself as member of the larger society. Positive identification with one's own ethnic group is a strong predictor of mental health and well-being in first- and second-generation immigrants ^{130,131,137}, particularly if they have a strong national identity as well ¹³⁸. Ethnic identity may buffer the negative consequences of racial discrimination ^{139,140}, and is likely to be weaker and more difficult to establish among members of ethnic minority groups who live isolated from their own ethnic group ¹⁴¹. The relationship between ethnic identity and schizophrenia has not been investigated.

Multiple levels of causation

Taken together, to date, the increased incidence of schizophrenia among immigrants has defied explanation, but the available evidence points towards social factors^{13,23,142}. More research that acknowledges and incorporates multiple levels of causation is needed¹⁴³. Differences in incidence between ethnic groups may be attributed to differences in the characteristics of the individuals who comprise the groups, but this approach is insufficient to fully understand the causes of incidence rates in the groups¹⁴⁴. Although diseases, including schizophrenia, are characteristics of individuals, causes need not be. At the end of the nineteenth century, the French sociologist Emile Durkheim tried to explain suicide rates across countries in Western Europe in terms of causes acting outside of the individual. He called these causes *social facts*, defined as “any way of acting ... capable of exerting over the individual an external constraint ... which is general over the whole of a given society, whilst having an existence of its own, independent of its individual manifestations”¹⁴⁵. Since then, several studies have shown that characteristics of neighborhoods or states influence the health of individuals^{146,147}.

Thus causes acting at the level of individuals, ethnic groups, neighborhoods and the population may all contribute to the individual risk of schizophrenia¹⁴³, as is illustrated by the neighborhood-level studies on ethnic density^{45,113}. Individual risk factors should therefore be studied in combination with ecological factors. Susser and Susser described this eco-epidemiological approach with the metaphor of Chinese boxes, “a conjurer’s nest of boxes, each containing a succession of smaller ones. Thus, within localized structures, we envisage successive levels of organization, each of which encompasses the next ..., all with intimate links between them”¹⁴³.

Outline and scope of this thesis

This thesis aims to advance our understanding of the increased incidence of schizophrenia among first- and second-generation immigrants, by investigating the social context of schizophrenia among immigrants both at the individual level and at the group level, and by studying aspects of acculturation as potential determinants of schizophrenia.

Specifically, the following research questions will be addressed:

Chapter 2: What is the incidence of schizophrenia among ethnic minorities in The Hague, the Netherlands? Which groups have an increased risk, and to what extent? Is the risk higher for second-generation immigrants than for those of the first generation?

Chapter 3: Are there any differences in the symptoms between immigrants and native Dutch people who make first contact for a psychotic disorder? Do these differences give any clues with regard to understanding the increased incidence of schizophrenia?

Chapter 4: Does the incidence of psychotic disorders among immigrants depend upon the social context of the neighborhood in which they live? Is the incidence higher in those immigrants who live in a neighborhood with a lower proportion of members of their own ethnic group?

Chapter 5: There is considerable heterogeneity across immigrant groups in incidence of schizophrenia. Is the incidence in ethnic minorities associated with the extent to which these groups perceive being the object of discrimination?

Chapter 6: Differences in degree of perceived discrimination between ethnic minority groups may influence their risk of schizophrenia (Chapter 5). Within an ethnic group, however, individual perceptions of discrimination vary, and may influence disease risk. Is discrimination a risk factor for schizophrenia at the individual level? Which demographic, social and psychological factors are associated with perceived discrimination?

Chapter 7: Ethnic identity strongly influences the mental health of ethnic minorities. Are lack of cognitive identification with one's own ethnic group and negative affective ethnic identity determinants of schizophrenia among non-Western immigrants?

Chapter 8: Cannabis use probably increases the risk of developing psychosis, particularly in individuals with a genetic predisposition to psychosis. Did non-Western immigrants who developed schizophrenia use cannabis more often than their unaffected siblings and than unrelated controls? Is there evidence for a genotype-environment correlation? Does the association between cannabis and schizophrenia vary across ethnic groups?

Chapter 9: The main findings are summarized, important limitations are considered, the findings are compared with the existing literature, and the implications of the results for research, prevention and treatment are discussed.

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2

Incidence of schizophrenia among ethnic minorities in the Netherlands: a four-year first-contact study

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Abstract

There is only one previous report on the first-contact incidence of schizophrenia among immigrants in the Netherlands, which was based on a small number of cases, particularly for second-generation immigrants. We conducted another two-year first-contact incidence study in the same geographical area, combined the data of both studies and compared risks over all four years. The incidence of schizophrenia was increased for all first-generation non-Western immigrants. The risk was particularly high for second-generation immigrants: the age- and gender-adjusted incidence rate ratio was 5.8 (95% CI, 2.9-11.4) for Moroccans, 2.9 (1.6-5.0) for Surinamese, 2.3 (1.0-5.4) for Turks, and 3.5 (1.8-6.8) for immigrants from other non-Western countries.

Introduction

Studies from the United Kingdom and Scandinavia have reported a very high incidence of schizophrenia among several immigrant groups ^{1,2}. A two-year first-contact study in The Hague, the Netherlands, found an increased incidence of schizophrenia among immigrants from Surinam and among male immigrants from Morocco ³. The risks were not significantly increased for Moroccan or Turkish women, or for immigrants from Western countries. However, these results were difficult to interpret, because the number of cases was small, particularly for the second generation.

As the high schizophrenia incidence rates among immigrants are still poorly understood ⁴ and have been questioned ⁵⁻⁷, it is important to clarify which immigrant groups are at higher risk, and to what extent second-generation immigrants are affected. We therefore conducted a second two-year first-contact incidence study in The Hague and combined the results of both studies. We compared the risks of schizophrenic disorders (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) in immigrants with those of native Dutch persons.

Method

Classification of ethnicity

The municipality of The Hague classifies ethnicity according to citizens' country of birth and to that of their parents. Immigrants include both those who are foreign-born (first generation) and those who have at least one foreign-born parent (second generation). Seven categories of ethnicity are used: 1. Morocco, 2. Surinam, 3. Turkey, 4. the Netherlands Antilles, 5. Other non-Western countries, 6. Western or westernised countries (Western or Northern Europe, the former Yugoslavia, the USA, Canada, Australia, New Zealand, Japan or Israel), and 7. native Dutch (those who are Dutch-born and whose parents were also born in the Netherlands). The municipal authorities provided population data, including ethnicity, age (5-year groups) and sex, for the years of the study.

Subjects

The criteria for inclusion and exclusion were similar to those used in the World Health Organization Ten-Country Study ⁸. Subjects whose residence in The Hague was shorter than six months or who lived there illegally were excluded. The study was conducted in two periods (April 1, 1997 - April 1, 1999 and October 1, 2000 - October 1, 2002). There was collaboration with the local general practitioners, psychiatrists and residents in psychiatry, to access every possible case. Over the four years of the study, 394 citizens of The Hague aged 15-54 years made first contact with a physician for a (suspected)

psychotic disorder. Thirty three subjects were excluded because of a diagnosis of a substance-induced psychotic disorder, a psychotic disorder due to a somatic condition, or a non-psychotic disorder. Participants gave written informed consent for the study. The study was approved by the ethics committee of University Medical Center Utrecht.

Diagnostic protocol

The patients were interviewed by Dutch residents in psychiatry (first study: JDB and NV; second study: WV), using the Dutch translation of a semi-structured diagnostic interview, the Comprehensive Assessment of Symptoms and History (CASH) ⁹. Relatives were interviewed by trained nurses (N = 4) using the Instrument for the Retrospective Assessment of the Onset of Schizophrenia (IRAOS) ¹⁰. In addition, the residents asked the treating physicians for detailed clinical information. Using information derived from CASH, IRAOS and the medical file, the residents compiled a narrative history of the patient's illness. For the patients who refused the interviews, they constructed a history using anonymised information from the responsible physician. During a diagnostic meeting, two psychiatrists made a consensus DSM IV diagnosis on the basis of the narrative history.

Blinding for ethnicity

During the first period (1997-1999) the psychiatrists who made the DSM IV diagnosis were blind for ethnicity, because any clue to a patient's ethnicity had been omitted from the narrative history, to ensure that their perceptions of immigrants would not influence their diagnoses. During the second period (2000-2002), information about the patient's ethnicity was included. The psychiatrists could thus take into account culturally based phenomena that could be mistaken for psychopathology.

Data analysis

For the analysis of the combined data, the numbers of cases from the two periods were added, as were the numbers of person-years. First-contact rates were calculated by dividing the number of cases by the number of person-years (ages 15 to 54). Incidence rate ratios (IRR) of schizophrenic disorders, adjusted for (five-year) age-group and sex, and 95% confidence intervals (95% CI) were calculated by Poisson regression analysis, using the STATA statistical program, version 9.0.

Results

First period, 1997-1999

The results of the first period have been reported previously ³.

Table 2.1 Incidence rate ratios (IRRs) of first contact for schizophrenic disorders^a in ethnic groups in The Hague, April 1, 1997 to April 1, 1999 plus October 1, 2000 to October 1, 2002.

Population segment	Person-years at risk		Schizophrenic disorders				
			Cases		IRR ^b (95%CI)		Gender-adjusted
	Male	Female	Male	Female	Male	Female	
First generation, aged 15-54 years							
Immigrants, total	172070	162143	74	28	2.3 (1.6-3.3)	2.1 (1.2-3.6)	2.3 (1.7-3.0)
Moroccans	22212	17480	24	1	5.2 (3.2-8.4)	0.6 (0.1-4.6)	4.0 (2.5-6.3)
Surinamese	43486	47183	15	13	2.1 (1.2-3.7)	3.6 (1.8-7.0)	2.6 (1.7-4.0)
Netherlands Antilleans	9036	9311	4	1	2.2 (0.8-5.9)	1.2 (0.2-9.1)	1.9 (0.8-4.6)
Turks	29199	23592	8	3	1.4 (0.7-2.9)	1.4 (0.4-4.7)	1.4 (0.7-2.6)
Others, non-Western ^c	44488	39874	19	7	2.3 (1.4-3.9)	2.1 (0.9-4.9)	2.2 (1.4-3.5)
Western or westernised ^d	23649	24703	4	3	1.0 (0.4-2.7)	1.5 (0.5-5.1)	1.2 (0.5-2.5)
Native Dutch ^e	316908	305822	55	24	1.0	1.0	1.0
Second generation, aged 15-54 years							
Immigrants, total	39288	38665	33	15	2.2 (1.4-3.5)	3.3 (1.6-6.6)	2.5 (1.7-3.7)
Moroccans	2919	3075	9	1	6.8 (3.3-14.1)	2.4 (0.3-17.9)	5.8 (2.9-11.4)
Surinamese	10121	9942	10	5	2.5 (1.2-5.0)	3.9 (1.4-10.6)	2.9 (1.6-5.0)
Netherlands Antilleans	1687	1582	1	0	1.9 (0.3-14.1)	n.a.	1.4 (0.2-10.4)
Turks	4721	4685	4	2	2.0 (0.7-5.6)	3.2 (0.7-13.9)	2.3 (1.0-5.4)
Others, non-Western	6397	6348	5	5	2.3 (0.9-5.8)	6.9 (2.5-18.5)	3.5 (1.8-6.8)
Western or westernised	13443	13033	4	2	1.5 (0.6-4.2)	1.8 (0.4-7.8)	1.6 (0.7-3.7)
Native Dutch	316908	305822	55	24	1.0	1.0	1.0

^a Includes DSM IV categories schizophrenia, schizophreniform disorder and schizoaffective disorder.^b Adjusted for age.^c Born in any country other than d and e.^d Born in Western, Northern, or Southern Europe (including the former Yugoslavia), the USA, Canada, Australia, New Zealand, Japan or Israel.^e Born in the Netherlands and both parents born in the Netherlands.

Second period, 2000-2002

One hundred ninety-seven subjects made first contact during this two-year period. Diagnostic interviews were conducted in 155 cases (78.7 %) and interviews with key informants in 132 cases (67.0 %). A consensus DSM IV diagnosis could be made for all but one subject. One hundred nineteen subjects (87 men, 32 women) were diagnosed with a schizophrenic disorder. Among these 119 subjects, the mean age at first contact was 26.7 years (SD, 8.0) for men and 27.9 years (SD, 9.0) for women. The crude first-contact

rate for schizophrenic disorders was 22.1 (95% CI, 19.3-25.0) per 100,000 population. For Dutch natives, this rate was 12.7 (95% CI, 9.9-15.5) per 100,000 population.

Periods combined, 1997-1999 and 2000-2002

Table 2.1 shows the age-adjusted incidence rate ratios for the immigrant groups, by sex and generation. Among immigrants from non-Western countries (Morocco, Surinam, Turkey, the Netherlands Antilles and Other non-Western countries combined), the incidence rate was significantly higher for the second generation than for the first (age- and gender-adjusted IRR, 1.53; 95% CI, 1.02-2.31).

Discussion

The risk for schizophrenic disorders was increased for first- and second-generation immigrants from Morocco, Surinam, and Other non-Western countries. Second-generation immigrants from these groups had higher risks than those of the first generation.

Remarkably, whereas the risk was very high for first- and second-generation Moroccan males, the risk for Moroccan females, first or second generation, was not significantly increased. We have no ready explanation for the low number of Moroccan women with a schizophrenic disorder, but the reason is unlikely to be that they avoid the mental health services. They visit their general practitioner more often than Dutch women do ¹¹, they are only somewhat less frequently in contact with the outpatient departments of psychiatric services than Dutch women are and more often than Surinamese or Antillean women ¹².

Comparisons between the first and the second period

The first-contact rate of schizophrenic disorders obtained in the second study (22 per 100,000; 95% CI, 19-27) was not significantly higher than that of the first (21 per 100,000). The IRRs for immigrants groups obtained in both studies were similar, and their confidence intervals overlapped.

Strengths and limitations

A strength of our study is the reliability of both the numerators (cases) and the denominators (person-years). The incident cases were derived from all sources of treatment in a defined geographical area. The person-years were derived from a comprehensive municipal registration system. Registration with municipal authorities is compulsory for all individuals residing legally in the Netherlands and a prerequisite for obtaining essential documents and financial aid (e.g. income support).

A second strength of both studies is the use of two different diagnostic methods. The psychiatrists who made the diagnosis during the first study were not involved in the treatment of the patients. Consequently, the researchers could keep them blind for ethnicity. During the second study, the same diagnostic protocol was used, with the only modification that the diagnoses were made by the responsible psychiatrists, who knew the patients well and were aware of their cultural background. Thus, we could explore the possibility that Dutch psychiatrists have a tendency to overdiagnose schizophrenic disorders in non-Dutch subjects. There was no evidence of this, because the proportions of immigrants that received a diagnosis of a schizophrenic disorder were similar in both the first and second periods (65% and 71% respectively; Pearson χ^2 , 0.76; $df = 1$; $p = 0.38$).

A possible limitation of the study is that the diagnostic interviews were conducted by native Dutch residents, who were not familiar with all the cultures of the subjects. However, semi-structured interviews have been shown to minimize misdiagnosis of immigrant patients¹³. In addition, when asked (in the first period of the study), the large majority of relatives viewed the symptoms as clearly abnormal.

Mechanism

Hypotheses to explain the findings must take into consideration that the rates of schizophrenia were increased in both first- *and* second-generation immigrants. Hypotheses which include psychosocial factors are therefore more viable than hypotheses that focus on a single biological or genetic factor.

Given the reports elsewhere of extremely high risks for black immigrants¹, it is of interest that the highest risk obtained in this study applies to a non-black minority group, i.e., Moroccan males. Moroccan immigrants to the Netherlands have greater difficulties in their process of acculturation to Dutch society than Surinamese or Antillean immigrants and their relationship with the Dutch population has become increasingly problematic¹⁴. This suggests that the experience of social defeat¹⁵ and acculturative stress¹⁶ might be important factors here. These concepts, encompassing experiences of a subordinate position, 'outsider status'¹⁵, marginalization, perceived discrimination, and a weak ethnic identity¹⁶ are likely to operate increasingly across both generations of immigrants.

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3

Symptoms at first contact for psychotic disorder: comparison between native Dutch and ethnic minorities

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Abstract

The incidence of schizophrenia and other psychotic disorders is very high among several ethnic minority groups in the Netherlands, and is most increased for Moroccans. This study compared symptoms at first treatment contact for a psychotic disorder between 117 native Dutch and 165 ethnic minority patients from Morocco, Surinam, Turkey, other non-Western countries and Western countries, using data from an incidence study for psychotic disorders over four years in The Hague, the Netherlands (1997-1999 and 2000-2002).

Patients were examined using the Comprehensive Assessment of Symptoms and History (CASH), which includes the Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS), and a section on DSM IV mood disorders. Differences between native Dutch and ethnic minorities in SAPS, SANS, total psychopathology (SAPS plus SANS), proportions of patients meeting the criteria for a current manic or depressive episode, and differences in individual symptoms were investigated using regression analyses.

Moroccans had higher total psychopathology and total SANS scores than native Dutch, and particularly presented more often with persecutory delusions. Moroccans and Turks more often met the criteria for a depressive episode. The other ethnic groups did not differ from native Dutch in levels of psychopathology.

These results suggest that Moroccans not only have the highest risk of schizophrenia of all ethnic groups in The Hague, but that they are also more severely ill at first treatment contact. Experiences of social adversity, which have been associated with persecutory delusions, and cultural factors may contribute to the observed differences in severity and content of psychopathology between Moroccans and native Dutch.

Introduction

The incidence of schizophrenia and other psychotic disorders is very high among several ethnic minority groups in north-western Europe^{1,2}. We have previously reported an increased risk for non-Western ethnic minority groups in The Hague, the Netherlands, which was most marked for Moroccan males³, and was associated with ethnic minority groups' experiences of discrimination⁴. Although there is some evidence that adverse social experiences, such as socioeconomic disadvantage, social defeat, racial discrimination or social isolation^{1,5-8}, may contribute to the increased risk for ethnic minorities, these findings are still poorly understood.

Research of psychotic phenomenology may elucidate mechanisms through which social factors are linked to psychotic disorders, as ethnic differences in symptomatology may reflect not only cultural, but also socio-environmental pathoplastic influences^{9,10}. Some recent studies suggested that adverse social experiences may lead to psychotic symptoms, particularly to paranoid ideations and persecutory delusions¹¹⁻¹³. There has not been any previous research on ethnic differences in psychotic symptomatology in the Netherlands, and studies from the US and UK have reported mixed results. Some studies did not find large differences across ethnic groups^{14,15}, while other studies did^{10,16-19}, suggesting that hallucinations, paranoid and religious delusions, as well as manic symptoms may be more common in patients from certain ethnic minority groups. A key problem in most of these studies was that they did not concern first-contact patients. Symptoms may have changed over the illness course or may have been influenced by previous treatment.

In the present study, we compared symptoms at first treatment contact for a psychotic disorder between native Dutch and ethnic minority groups in the city of The Hague, the Netherlands. Data were collected during a first-contact incidence study of psychotic disorders over four years (1997-1999 and 2000-2002)³. While the overall aim of this study was exploratory, we hypothesized that ethnic minority patients in general and Moroccans in particular would have more persecutory delusions than native Dutch patients.

Method

Classification of ethnicity

The municipality of The Hague keeps records of citizens' country of birth and that of their parents. In this study, we used the classification of ethnicity as defined by the Netherlands' Bureau of Statistics. Dutch ethnicity is assigned to citizens who are Dutch-born and

whose parents were also born in the Netherlands (hereafter referred to as native Dutch). If a citizen, or (one of) his or her parents, was born abroad, he or she is assigned to the group of people born in the same country. If the parents were born in different foreign countries, the country of birth of the mother determines the assignment to a particular group. Since they share the background of their country of origin, immigrants and their children are assigned to the same group. Foreign countries of birth are condensed into six categories: 1. Morocco, 2. Surinam, 3. Netherlands Antilles, 4. Turkey, 5. Western or westernized countries (northern, southern or western Europe, the former Yugoslavia, the USA, Canada, Australia, New Zealand, Japan or former Netherlands East Indies), 6. All other (non-Western) countries. On January 1, 2002, the city of The Hague had 457,674 inhabitants, of whom 42.8 % was foreign-born or had a foreign-born parent.

Identification of cases

Every citizen of The Hague aged 15-54 years who made first contact with a physician for a possible psychotic disorder over four years (April 1, 1997 - April 1, 1999 and October 1, 2000 – October 1, 2002) was considered a possible case. The study team had regular contact with more than 200 local general practitioners throughout the city, and with the psychiatrists and residents in psychiatry of the single mental health organization in The Hague, to get access to every possible case. The inclusion criteria were similar to those used in the World Health Organization (WHO) Ten-Country study²⁰: age between 15 and 54 years; resident within The Hague; presence of any DSM IV criterion A symptom of schizophrenia, or clinical suspicion of psychosis; and no previous contact with health services for psychosis. Subjects who met these criteria according to the study team were asked to participate in diagnostic interviews.

The study was approved by the ethics committee of University Medical Center Utrecht. In the first period, the protocol was used primarily for research purposes²¹; in the second period, patients were being identified for inclusion in an early psychosis treatment service, and the protocol was used for this service.

Assessment of psychopathology

Interviews were conducted by three native Dutch residents in psychiatry, using the Dutch translation of a semi-structured diagnostic interview, the Comprehensive Assessment of Symptoms and History (CASH)²². They had completed a training in the CASH. This interview includes the Scale for the Assessment of Positive Symptoms (SAPS, with 34 items measured on an ordinal scale ranging from 0 [absent] to 5 [severe])²³ and the Scale for the Assessment of Negative Symptoms (SANS, with 21 items)²⁴. Current mood symptoms, derived from the DSM IV criteria for mania and depression, were rated dichotomously as present or absent. The presence of mood disorders was assessed ac-

ording to whether patients met the criteria as defined in DSM IV. We did not examine the interrater reliability for SAPS, SANS or mood symptoms.

Using information derived from CASH, a semi-structured interview with relatives (the Instrument for the Retrospective Assessment of the Onset of Schizophrenia [IRAOS] ²⁵) and the medical file, the residents compiled a narrative history of the patient's illness. For the patients who refused the interviews, they constructed a history using anonymised information from the responsible physician. During a diagnostic meeting, two psychiatrists made a consensus DSM IV diagnosis on the basis of the narrative history. Following the exclusion criteria of the WHO study, patients who were diagnosed with a substance-induced psychotic disorder, a psychotic disorder due to a somatic condition or a non-psychotic disorder, were excluded.

Statistical analysis

Stata statistical program version 9.1 was used for all analyses. Total SAPS and total SANS scores were calculated by adding the scores of the individual items of the scales. Total psychopathology was measured as the sum of the SAPS and SANS scores. The mean scores of the three scales were compared between native Dutch and ethnic minority patients using linear regression analyses, with psychopathology scale scores as dependent variables and ethnicity, age and sex as independent variables. Proportions of patients meeting the DSM IV criteria for current mood episodes were calculated. Logistic regression was used to examine ethnicity as predictor for current episode of mania and depression.

Next, we focused on individual symptoms. Since the distributions of scores were very skewed, and transformations did not yield normal distributions, for each SAPS and SANS item a dichotomous score was calculated, with scores 0 (absent) and 1 (dubious) as 'absent' and scores 2 (mild) to 5 (severe) as 'present'. The prevalence of individual symptoms was calculated in each ethnic group. First, we examined differences in the prevalence of persecutory delusions between native Dutch and the ethnic minority groups, using logistic regression. Odds Ratios (OR) and 95% Confidence Intervals (95% CI) were calculated. Second, the other positive, negative and mood symptoms were analyzed. To reduce the number of statistical tests, differences between native Dutch and ethnic minority groups were investigated only if there were statistically significant differences on the total SAPS, total SANS or total psychopathology scale scores.

All associations were adjusted for age and sex and tested for statistical significance using Wald tests (F tests in case of linear regression analyses and χ^2 tests in logistic regression analyses) ²⁶.

Results

Over the four years of the study, 415 citizens aged 15-54 years made first contact with a physician in The Hague for a suspected psychotic disorder. Twenty one subjects were excluded because they had a prior history of contact for a psychotic disorder or because they did not stay (legally) in The Hague. Thirty three were excluded because of a diagnosis of a substance-induced psychotic disorder, a psychotic disorder due to a somatic condition, or a non-psychotic disorder (20 ethnic minority subjects and 13 native Dutch). The remaining 361 patients consisted of 223 first- or second-generation ethnic minority patients and 138 patients with native Dutch ethnicity. Diagnostic interviews were administered to 282 (78 %) patients. Members of ethnic minorities participated less often in the interviews than native Dutch did (74% and 85% respectively, $\chi^2 = 5.81$, $df=1$, $p=0.02$). Some patients were unable to complete the interview or refused to do this. Information on mood symptoms, assessed in the last part of the interview, was available for 250 (69 %) patients. The proportion of those who did not complete the section of mood symptoms was similar in the native Dutch group ($n=9$ [8%]) to that in the ethnic minority group ($n=23$ [14%], $\chi^2 = 2.66$, $df=1$, $p=0.10$). Characteristics of the study sample are shown in Table 3.1.

Table 3.1 Characteristics of study sample.

	Ethnic minorities ^a N=223		Native Dutch N=138		test	p-value
Mean age (SD)	27.95	(8.80)	29.97	(9.26)	$t=2.08$	0.038
Male sex, No. (%)	161	(72)	89	(64)	$\chi^2=2.38$ (1)	0.123
Level of education, No. (%) ^b						
No education	9	(5)	0	(0)		
Primary school	26	(13)	3	(2)	$\chi^2=20.46$ (3)	0.000
Secondary school	134	(68)	99	(76)		
Higher education	27	(21)	29	(22)		
First generation, No. (%)	157	(70)	-			
CASH interview, No. (%)	165	(74)	117	(85)	$\chi^2=5.81$ (1)	0.016
DSM IV diagnosis, No. (%)						
Schizophrenia spectrum disorder	151	(68)	78	(57)		
Depressive disorder	9	(4)	7	(5)	$\chi^2=9.61$ (5)	0.087
Bipolar disorder	11	(5)	13	(9)		
Delusional disorder	4	(2)	2	(1)		
Brief psychotic disorder	11	(5)	16	(12)		
Not otherwise specified	37	(16)	22	(16)		

^a All patients but those with Dutch ethnicity, includes first and second generation.

^b Information missing for 34 (9%) patients.

Table 3.2 Severity of psychopathology in patients from different ethnic groups making first contact for a psychotic disorder ^a.

Ethnic group	Psychopathology				
	Mean (SD)			N (%)	
	Total ^b	SAPS	SANS	Mania ^c	Depression ^d
All ethnic minorities	57.97 (27.94)	33.25 (18.90)	24.53 (17.71)	7 (5.0)	33 (23.2)
Morocco	65.15 (27.89) ^e	35.77 (19.29)	29.38 (18.59) ^e	1 (3.3)	14 (42.4) ^f
Surinam	54.97 (27.25)	32.61 (20.46)	22.36 (15.74)	1 (3.2)	1 (3.2)
Turkey	53.91 (30.65)	27.36 (14.73)	26.55 (20.32)	0 (0.0)	8 (38.1) ^e
Western countries	52.45 (21.75)	32.00 (13.00)	20.45 (18.88)	1 (9.1)	2 (18.2)
Other countries	56.76 (28.34)	34.61 (20.29)	22.14 (16.49)	4 (8.7)	8 (17.4)
Native Dutch	51.91 (26.98)	30.84 (18.77)	21.06 (16.55)	11 (10.2)	21 (19.4)

^a All comparisons tested for statistical significance with Wald tests, in linear or logistic regression models, adjusted for age and sex, with native Dutch as reference group.

^b SAPS and SANS score added.

^c Patients meeting the DSM IV criteria for current manic episode.

^d Patients meeting the DSM IV criteria for current depressive episode.

^e $p < 0.05$

^f $p < 0.005$

The total SAPS scores of the study sample ranged from 0 to 94, SANS scores from 0 to 72, total psychopathology from 5 to 148. The mean scores of the three scales were similar for all ethnic minority patients combined and native Dutch (Table 3.2). Comparisons between native Dutch and the separate ethnic groups yielded statistically significant differences with Moroccans, for total psychopathology (51.91 versus 65.15, age- and sex-adjusted $F [1,144] = 3.96$, $p = 0.048$) and for total SANS (21.06 versus 29.38, adjusted $F [1,145] = 4.48$, $p = 0.036$) (Table 3.2).

Ethnic minority patients met the DSM IV criteria for a manic episode somewhat less often than the native Dutch patients did, but the reverse was true for a major depressive episode (Table 3.2). After adjustment for age and sex, these differences were statistically significant for the prevalence of depression among Moroccans (OR = 4.00, 95% CI, 1.58-10.15, $p = 0.004$) and Turks (OR = 3.07, 95% CI, 1.08-8.75, $p = 0.04$).

The prevalence of persecutory delusions was higher in the ethnic minority patients than in the native Dutch patients (59% versus 47%, age- and gender-adjusted OR = 1.68, 95% CI, 1.02-2.76, $p = 0.04$). When each ethnic group was compared to the native Dutch group separately, the odds were increased for all ethnic minority groups, but the increase was statistically significant for Moroccans only (OR = 3.44, 95% CI, 1.49-7.93, $p = 0.004$) (Table 3.3).

Table 3.3 Differences in positive, negative and mood symptoms between Moroccan and native Dutch patients making first contact for a psychotic disorder.

	Moroccans %	Native Dutch %	Unadjusted		Adjusted ^a	
			OR	95 % CI	OR	95 % CI
Positive symptoms ^b						
Persecutory delusions	74	47	3.32	1.49-7.43	3.44	1.49-7.93
Bizarre behavior	59	32	3.03	1.43-6.41	3.14	1.43-6.87
Visual hallucinations	44	21	2.84	1.31-6.15	3.08	1.36-7.00
Religious delusions	8	23	0.28	0.08-0.98	0.29	0.08-1.06
Negative symptoms ^b						
Anhedonia, relationships	62	37	2.74	1.30-5.80	2.69	1.23-5.90
Alogia, poverty of speech	38	21	2.40	1.09-5.26	2.61	1.12-6.09
Avolition, grooming and hygiene	44	22	2.70	1.25-5.83	2.31	1.04-5.12
Mood symptoms ^c						
Diminished interest or pleasure	68	48	2.32	0.99-5.42	2.78	1.15-6.74
Inflated self-esteem	4	16	0.14	0.02-1.09	0.11	0.01-0.88

^a Adjusted for age and sex, native Dutch as reference category.

^b Positive symptoms from SAPS, negative symptoms from SANS; N=39 in Moroccan group, N=117 in native Dutch group.

^c DSM IV diagnostic criteria for depressive and manic episodes; N=33 in Moroccan group, N=108 in native Dutch group.

Table 3.3 shows all individual positive, negative and mood symptoms that differed significantly between Moroccan and native Dutch patients. Out of 64 symptoms, seven symptoms were significantly more prevalent in the Moroccan group. Differences were largest with regard to persecutory delusions, but also included bizarre behaviour (OR = 3.14, 95% CI, 1.43-6.87, $p = 0.004$) and visual hallucinations (OR = 3.08, 95% CI, 1.36-7.00, $p = 0.007$). Native Dutch more often presented with religious delusions and inflated self-esteem.

Discussion

First- and second-generation immigrants from Morocco who made first treatment contact for a psychotic disorder in The Hague had significantly higher total psychopathology and negative symptom scores than the native Dutch patients had, and particularly more often presented with persecutory delusions, bizarre behavior and visual hallucinations. Also, Moroccan and Turkish patients more often met the criteria for a current depressive episode. Other ethnic minority groups had levels of psychopathology similar to those in native Dutch.

Social adversity

Of all ethnic minority groups in The Hague, immigrants from Morocco experience the highest level of social adversity, including the lowest socioeconomic status and the highest degree of discrimination²⁷⁻²⁹. We have previously reported that the incidence of psychotic disorders varied across ethnic minority groups by degree of perceived discrimination: incidence was higher when the group experienced more discrimination⁴. Cognitive psychological models of the development of psychosis postulate that such experiences may create an enduring cognitive vulnerability, which is characterized by negative schematic models of the self and the world, e.g. beliefs about the self as vulnerable to threat, or about others as dangerous¹¹. This vulnerability has been associated with depression, and may lead to paranoid ideations and in extreme form to persecutory delusions in those genetically at risk for psychosis^{11-13,30}. In studies of non-psychotic individuals, higher levels of paranoia were associated with perceived racism³¹ and with lower perceived social rank³².

Cultural factors

Occurrence and content of psychotic symptoms may be influenced by cultural background^{10,33,34}. Belief in witchcraft is very common in Moroccan culture³⁵, which may be associated with the tendency to attribute misfortune and negative events to evil spirits (*djinn*s) or malevolent people. In addition, the Moroccan-Berber culture has been described as guarded and distrustful³⁵. Thus, persecutory delusions may not have the same clinical significance as in native Dutch and may be part of the Moroccan idiom of distress³⁴. The higher prevalence of visual hallucinations among Moroccan patients may also be influenced by cultural factors. Since hallucinatory experiences are more positively valued in some non-western cultures, they may be more frequently noticed and communicated to others³³. It is unlikely, however, that the observed ethnic differences in symptoms are entirely explained by cultural influences, because other non-Western ethnic minorities did not differ significantly from native Dutch in symptomatology. In addition, the proportion of Moroccans with religious delusions was somewhat lower than that of native Dutch (Table 3.3). There may be an interplay between culture and adverse social experiences in the development and expression of psychopathology. Individuals with Moroccan background may be more inclined to paranoid ideations, and when confronted with social adversity, they may be more likely to develop persecutory delusions and depression.

Previous findings

Since most previous studies did not concern first-contact samples, it is difficult to interpret these findings. However, similar to our results, several studies reported a higher prevalence of paranoid symptoms in various ethnic minority groups than in indigenous

populations^{10,17-19}. This cross-cultural finding suggests that paranoid symptoms may develop within the context of social adversity associated with ethnic minority status, and can not be entirely explained by cultural background.

Other inter-ethnic differences in psychopathology have been reported less consistently, such as higher rates of first rank symptoms among African-Americans in the USA^{16,36}, religious delusions among African-Caribbeans and Asians in the UK^{10,19}, manic-catatonic symptoms among African-Caribbeans in the UK¹⁵, and worrying or somatic concerns in Asians in the UK¹⁸ and Latinos in the US¹⁷. These findings may be attributed to the influence of cultural background in these specific groups, or to the selection of hospitalized or chronic patients.

Potential confounding factors

Moroccan patients may make contact with health services only when they are more severely ill. The duration of untreated psychosis (DUP), defined as the interval between psychosis onset and first contact with a physician, was assessed in the first period of this study²¹. There were no statistically significant differences in DUP across ethnic groups; the median DUP was 4.5 weeks (interquartile range 1-26) for Moroccans and 3.0 weeks (1-37) for native Dutch²¹. Thus, it is unlikely that longer DUP could account for the results. In addition, the short median DUP in Moroccan patients suggests that alternative treatment has not been an important reason for treatment delay.

The use of medication prior to symptom assessment may have influenced the results. Information on antipsychotic medication was available for the first period of the study. The majority of participants (62%) did not use antipsychotic medication or had used those shorter than one month. Of the Moroccan patients, 47% had used antipsychotic medication longer than one month (native Dutch: 25%, $\chi^2 = 3.08$, $df=1$, $p=0.08$). If anything, the higher prevalence of use of antipsychotics among Moroccan patients will have led to underestimation of differences in psychopathology, as the use of medication is likely to reduce psychotic symptoms.

Moroccans had a lower level of education than native Dutch. Although most previous research did not take level of education into account, one study found a significant effect of education on severity of psychotic symptoms¹⁷. It is difficult to understand the role of education in this respect, because a low level of education may reflect low socioeconomic status or social adversity, may be associated with lower perceived social status, with lower acculturation and with lower intelligence. When we further adjusted for level of education, the differences between Moroccan and native Dutch with regard to prevalence of persecutory delusions increased (OR = 4.44, 95% CI, 1.77-11.12) and remained statistically significant for prevalence of depression, bizarre behavior and

inflated self-esteem, whereas differences in total psychopathology, negative symptoms and visual hallucinations were attenuated and were no longer statistically significant.

Cannabis use has been associated with higher rates of psychotic symptoms³⁷. Among cases in the first period of our study, however, cannabis was used more often by native Dutch (23%) than by Moroccan patients (17%) prior to onset of psychosis³⁸.

Strengths and limitations

The present study included all patients making first contact for a psychotic disorder over four years, rather than a sample of hospitalized or chronic patients. This is a more appropriate design to study differences in psychopathology between ethnic groups, as symptoms are likely to change as a result of treatment and during the subsequent course of the illness.

We did not conduct a leakage study, which implies that we may have missed some cases. This may have influenced the results if there would be an association between the probability of being identified as a case and severity and content of symptoms, but only if this association would be different for Moroccan patients than for native Dutch patients. However, a recent large incidence study in the United Kingdom among different ethnic groups found that the cases identified in the leakage study they had conducted “were remarkably similar to those subjects identified in the initial survey”³⁹.

Immigrant patients refused the diagnostic interview more often than the native Dutch patients did (Table 3.1), perhaps because of cultural factors, such as stigma of psychiatric illness. Another possibility is that patients who did not participate were more severely ill. This hypothesis is supported by the finding that patients who agreed to be interviewed, but could not or would not finish the last part of the CASH which assessed mood symptoms, had significantly higher mean scores of total SAPS, total SANS and total psychopathology than those who completed the interview (statistical test for the latter: $t = 4.52$, $p < 0.001$). Consequently, the refusals are more likely to have led to an underestimation of psychopathology in immigrant patients than to an overestimation.

Missing CASH ratings for mood symptoms may have contributed to underdiagnosis of depressive and bipolar disorders, but this applies to the ethnic groups to a similar degree, as the proportions of those for whom there was no CASH information on mood symptoms did not differ significantly between the native Dutch patients and the immigrant patients.

We did not restrict our analysis to certain DSM IV diagnostic categories, because there is controversy around the cross-cultural diagnosis and classification of psychotic disorders^{36,40,41}. Although we used semi-structured diagnostic interviews with patients as well as with relatives, although blinding and non-blinding of psychiatrists to ethnicity yielded similar proportions of schizophrenia diagnoses³, and although diagnostic stability of schizophrenic disorders among the patients of the first study period (after two and half years) was very high (91%)⁴², there still may have been some misclassification of DSM IV diagnoses. The large proportions of Moroccan and Turkish patients meeting the criteria for a current depressive episode may be an indication of such misdiagnosis, but, considering the rigorous diagnostic protocol we have used, this finding is more likely to represent comorbidity of depression, which means that in spite of the current depressive episode, the diagnostic criteria for depressive disorder with psychotic features or schizoaffective disorder were not met. Nevertheless, these findings underscore the difficulties of making a diagnosis of psychotic disorders in different ethnic groups, and indicate that psychotic and depressive symptoms, as well as cultural background and ethnicity, have to be weighed carefully.

The small sample sizes prevented comparisons between first- and second-generation immigrants within each ethnic minority group. We were able to compare all first-generation immigrants with all second-generation immigrants. There were no statistically significant differences in psychopathology between the groups.

We did not adjust for multiple comparisons in the analyses of individual symptoms, because it has been questioned whether this method should be used in exploratory analyses⁴³. It implies that a given comparison will be interpreted differently according to how many other tests were performed, which is difficult to understand. In addition, in the comparisons of 64 individual symptoms, the number of type II errors would increase too much, as the adjusted significance level would have to be 0.0008⁴³.

Finally, symptoms were rated by native Dutch residents in psychiatry. Since they were not familiar with all aspects of the different cultures, they may have misinterpreted some expressions or behaviors in immigrants as psychopathological. However, cross-cultural misunderstanding is unlikely to account for the findings, because relatives of ethnic minority patients were asked whether they thought the symptoms were appropriate within their culture or not²¹. If relatives felt that a certain expression or behavior was not uncommon within their culture, the residents were cautious to rate this as psychopathology.

Conclusion

Moroccans have the highest risk of schizophrenia of all ethnic groups in The Hague³. The results of the present study suggest that they are also more severely ill at first treatment contact. The particularly high prevalence of depression and persecutory delusions in Moroccan patients underscore the importance of paying attention to depressive symptoms in ethnic minority patients with psychotic illness, and lend support to hypotheses linking social adversity to the development of psychosis. Thus, the findings also have broader implications in that they suggest that social context can play a role in etiology.

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Ethnic density of neighborhoods and incidence of psychotic disorders among immigrants

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Abstract

Objective: Previous studies have reported a very high incidence of psychotic disorders in immigrant ethnic groups in Western Europe. Some studies suggested that ethnic density may influence the incidence of schizophrenia. We investigated whether this increased incidence among immigrants depends upon the ethnic density of the neighborhoods in which they live.

Method: Incidence study of psychotic disorders in The Hague, by ethnicity and neighborhood of residence. Over a seven-year period individuals making contact with a physician for a suspected psychotic disorder were identified; diagnostic interviews were administered to these individuals; DSM IV diagnoses were assigned by consensus of two psychiatrists. A comprehensive municipal registration system provided the denominator. The study size was sufficient to examine incidence rates in immigrants from Morocco, Surinam and Turkey (first- and second-generation combined), and in native Dutch. The ethnic density of the neighborhood of residence was measured as the proportion of one's own ethnic group in the neighborhood. Multi-level regression analyses predicted incidence of psychotic disorders as a function of individual ethnicity and neighborhood ethnic density. Models were fitted for all immigrants together and for each immigrant group separately.

Results: There were 226 native Dutch and 240 immigrants diagnosed with a psychotic disorder. Compared to native Dutch, the adjusted incidence rate ratios for immigrants were 2.36 (95% CI, 1.89 to 2.95) in neighborhoods with low ethnic density and 1.25 (0.66 to 2.37) in neighborhoods with high ethnic density. There was a strong interaction between individual ethnicity and neighborhood ethnic density as predictors of incidence of illness (adjusted $\chi^2 = 15.04$, $df = 1$, $p = 0.0001$). These findings were consistent across all immigrant groups.

Conclusion: The incidence of psychotic disorders was increased most significantly among immigrants living in neighborhoods where their own ethnic group comprised a small proportion of the population.

Introduction

Schizophrenia is ranked by the World Health Organization as one of the leading causes of long-term disability¹. Like many complex disorders, it has both genetic and non-genetic causes, which remain largely unknown². A striking finding from epidemiological studies is the high incidence rate of schizophrenia and other psychotic disorders among several ethnic minority groups, mainly in Western Europe^{3,4}. A recent meta-analysis of 18 incidence studies of schizophrenia and other psychotic disorders estimated relative risks of 2.7 (95% Confidence Interval, 2.3-3.2) and 4.5 (1.5-13.1) for first- and second-generation immigrants respectively, compared with native populations⁵. While this finding may offer clues to the etiology of psychotic disorders, thus far it has defied explanation. High incidence rates in the countries of origin, selective migration, diagnostic bias, or variation in the frequency of putative risk factors such as cannabis use, obstetric complications, or exposure to viruses, do not account for the immigrants' elevated risk^{5,6}.

Increasingly, investigators suspect that the social experiences of immigrant groups after migration contribute to their elevated risk^{5,6}. However, few studies have collected data to test this hypothesis. One way to examine whether social experience influences risk is to test whether the increased incidence among immigrants depends upon the social context in which they live. The present study focused on the context of neighborhood ethnic density, which is pivotal in shaping the everyday social experience of ethnic minorities. In the United States, a landmark study in the 1930s reported higher hospital admission rates for schizophrenia among ethnic minorities who lived in neighborhoods with a low proportion of persons belonging to their own ethnic group⁷. Recently, this field of research was rejuvenated by a study in London⁸, which reported an increased incidence of schizophrenia for ethnic minorities who lived in neighborhoods with a low proportion of ethnic minorities. The London study provided stronger evidence for an ethnic density effect, using data from all mental health services rather than hospital admission data, but still, had some limitations, leaving room for the criticism that the ethnic density effect may be an artifact.

In The Hague, the Netherlands, the conditions were met to test whether the relationship between immigration and psychosis is dependent upon or modified by ethnic density, in a prospective first-contact incidence study of psychotic disorders over seven years, which yielded a large number of incident cases in one geographical area with several immigrant groups of sufficient size and reliable detailed population data.

Methods

Classification of ethnicity

The municipality of The Hague classifies ethnicity according to citizens' country of birth and that of their parents. Dutch ethnicity is assigned to citizens who are Dutch-born and whose parents were also born in the Netherlands (hereafter referred to as native Dutch). If a citizen was born abroad, he or she is assigned to the group of people born in the same country. A Dutch-born citizen is considered a second-generation immigrant if at least one parent was born abroad. If the parents were born in different foreign countries, the country of birth of the mother determines the assignment to a particular group. On January 1, 2005, the city of The Hague had 472,087 inhabitants, of whom 34.5% was a first- or second-generation immigrant from any non-Western country. For the present study, the three largest groups of first- and second-generation non-Western immigrants were included: Moroccans (24,144), Surinamese (45,388), and Turks (32,228). Thirteen percent of the population comprised more than 100 other non-Western ethnic groups. The proportion of these groups was less than five percent in all neighborhoods, which made it impossible to study ethnic density within these groups.

Characteristics of neighborhoods

The Hague consists of 44 neighborhoods, classified according to postal codes, with a maximum number of 38,000 inhabitants per neighborhood. The ethnic density of a neighborhood was computed for each immigrant group as the proportion of residents

Table 4.1 Characteristics of the neighborhoods of The Hague and distribution of cases across the neighborhoods.

Classification of neighborhood ethnic density	Neighborhood proportion of immigrants ^a	Number of neighborhoods	Socioeconomic level ^b		Cases	
			Mean	SD	Native Dutch ^c	Immigrants ^d
High ^e	> 0.65	2	-20.2	2.3	12	73
	0.40-0.65	4	-8.2	4.6	19	66
	0.30-0.40	6	-6.8	3.7	63	64
Low	0.20-0.30	5	2.4	8.5	32	11
	0.10-0.20	15	13.6	6.4	60	17
	< 0.10	12	12.2	7.9	38	8

^a Proportion of *all* non-Western immigrants in the neighborhood, average across study period.

^b Mean socioeconomic level of all neighborhoods in each stratum. Measure defined in text, 0 is average socioeconomic level of the city.

^c Those who are Dutch-born and whose parents were also born in the Netherlands.

^d First- and second-generation immigrants from Morocco, Surinam and Turkey.

^e *Group-specific* neighborhood ethnic density was highest in these two neighborhoods for each separate immigrant group.

belonging to that group. The analyses in this paper use only this group-specific measure of ethnic density.

Neighborhood deprivation, defined by high proportions of unemployed persons, low average income, poor quality of housing and high crime rates, negatively influences health ⁹, and has been associated with high rates of schizophrenia in some studies ¹⁰. Therefore, investigations of ethnic density should take neighborhood deprivation into account. A measure of the socioeconomic level of the neighborhoods was provided by the municipality. This score is based on proportion long-term unemployed, average income, quality of housing, and mean level of education (but not proportion of ethnic minorities). The average socioeconomic level of the city has been set as zero; scores of the neighborhoods ranged from -21.8 to 26.9.

The distribution of cases across neighborhoods is shown in Table 4.1. Non-Western immigrants clustered in deprived neighborhoods; there was a strong negative correlation between proportion of immigrants and socioeconomic level of a neighborhood (Pearson correlation coefficient = -0.71, $p < 0.0005$). The highest concentrations of non-Western immigrants were found in the two most deprived neighborhoods, where the proportion of all non-Western immigrants, averaged across the years of the study, was 82.6 %. Ethnic density of the separate large ethnic minority groups was highest in these two neighborhoods as well, and was 16.8 % for Moroccans, 23.9 % for Surinamese, and 26.3 % for Turks. Since proportions of non-Western immigrants in other neighborhoods

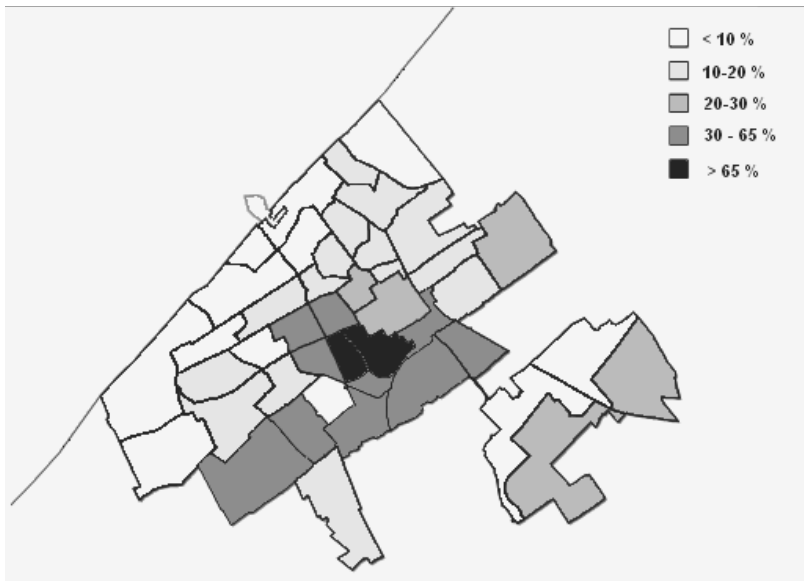


Figure 4.1 The 44 neighborhoods of The Hague and distribution of non-Western immigrants, average proportion across neighborhoods over the years of the study.

were considerably smaller (Figure 4.1), we classified these two neighborhoods as high ethnic density and the other 42 neighborhoods as low ethnic density.

Identification of cases

A first-contact incidence study over seven years (April 1, 1997 - April 1, 1999 and October 1, 2000 – October 1, 2005) sought to identify and diagnose every citizen of The Hague aged 15-54 years who made first contact with a physician for a possible psychotic disorder. Previous reports have detailed the methods of this study and presented descriptive data on incidence rates up to 2002 ^{4,11}. Briefly, the criteria for a possible psychosis were similar to those used in the World Health Organization Ten-Country study of the incidence of psychotic disorders ¹². There was extensive collaboration with the local general practitioners, psychiatrists and residents in psychiatry, in the effort to identify every possible case. Except in the first two years, when the protocol was used primarily for research purposes ¹¹, patients were being identified for inclusion in an early psychosis treatment service.

Patients with possible psychosis were referred to the early psychosis department for evaluation and treatment. They were interviewed by Dutch residents in psychiatry, using a semi-structured diagnostic interview, the Comprehensive Assessment of Symptoms and History (CASH) ¹³. Relatives were interviewed by trained nurses, using the Instrument for the Retrospective Assessment of the Onset of Schizophrenia (IRAOS) ¹⁴. If necessary, an official interpreter was available to help in the administration of CASH or IRAOS. In addition, the residents asked the physicians of the patients for detailed clinical information. Based on CASH, IRAOS and clinical information, the residents compiled a narrative history of the patient's illness. For patients who could not be evaluated in this way (e.g. refused a full diagnostic interview), a history was made with the anonymized clinical information. During a diagnostic meeting, two psychiatrists made a consensus DSM IV diagnosis on the basis of the narrative history.

Using this protocol, we identified 678 patients with a possible psychotic disorder over 1,870,408 person-years of observation. 522 (77%) received a full evaluation and 156 (23%) were diagnosed based on anonymized clinical information.

Based on the consensus diagnoses, 60 patients were excluded, due to a diagnosis of a substance-induced psychotic disorder, a psychotic disorder due to a somatic condition or a non-psychotic disorder. Among the remaining 618 cases, there were 466 cases with Moroccan, Surinamese, Turkish or Dutch ethnicity, used in the present analysis. Postal code of the subjects was documented at first contact.

Other municipal data

The municipal authorities also provided population data for the years of the study, including neighborhood, age, sex, marital status, and ethnicity.

Statistical analysis

In order to take the two-level grouping structure of the data (individuals clustered in neighborhoods) into account, the XTPOISSON multi-level Poisson regression modeling procedure in the Stata statistical program was used¹⁵. For each individual, the proportion of own ethnic group in the neighborhood was used as the measure of ethnic density. To obtain count data, individual data were aggregated by sex, eight five-year age groups (15-54 years), marital status (single or other), neighborhood socioeconomic level, the four categories of ethnicity, and neighborhood ethnic density. The model used in the analysis of ethnicity and ethnic density was adjusted for the fixed effects of all aggregated predictors. A neighborhood-specific random intercept, having a gamma distribution, was included in the model. Main effects and interactions were tested for statistical significance by Wald tests¹⁶.

First, we carried out indirect standardisation with the rates of psychotic disorders for the total seven-year population as the standard and applied them to each neighborhood, stratifying for age, sex, marital status and ethnic minorities using the Stata ISTDIZE procedure. The standardisation used the stratum specific rates of the standard population to calculate the expected number of cases for each neighborhood and the adjusted incidence rates at neighborhood level. We calculated the standardised incidence ratio (SIR) by dividing the number of cases observed by the expected number⁸.

Second, we examined the fixed effects of individual ethnicity on the incidence of psychotic disorders. We calculated incidence rate ratios (IRR) and 95% Confidence Intervals (95% CI) for psychotic disorders with native Dutch as the reference category.

Third, we used a stratified analysis to examine whether the effect of individual ethnicity was modified by ethnic density. The effect of individual ethnicity on the incidence of psychotic disorders was computed separately for immigrants living in high and low ethnic density neighborhoods. This was done for all immigrant groups together and for each immigrant group. Effect sizes from the interactions were calculated, fitted with this two-level variable, using the appropriate linear combinations in the Stata LINCOM command. Fourth, the continuous variable of neighborhood ethnic density was used. The interaction between individual ethnicity and ethnic density was included in the multi-level model.

Table 4.2 Sociodemographic characteristics and diagnoses of individuals making first contact for a psychotic disorder in The Hague, 1997-2005.

	Native Dutch ^a		Immigrants ^b		Total	
	No.	%	No.	%	No.	%
Patients	226	48	240	52	466	100
Gender						
Male	157	69	173	72	330	71
Female	69	31	67	28	136	29
Age, years						
15-34	176	78	203	85	379	81
35-54	50	22	37	15	87	19
Diagnosis						
Schizophrenia spectrum disorder ^c	142	63	179	75	321	69
Major depressive disorder with psychotic features	9	4	11	4	20	4
Bipolar disorder with psychotic features	20	9	6	2	26	6
Delusional disorder	4	2	2	1	6	1
Brief psychotic disorder	19	8	9	4	28	6
Psychotic disorder, not otherwise specified	32	14	33	14	65	14

^a Those who are Dutch-born and whose parents were also born in the Netherlands.

^b First- and second-generation immigrants from Morocco, Surinam and Turkey.

^c Includes DSM IV categories schizophrenia, schizophreniform disorder, and schizoaffective disorder.

Additional analyses addressed the potential for bias due to differences in case ascertainment in high versus low ethnic density neighborhoods. If immigrants were more averse to seeing a physician in high than low ethnic density neighborhoods, we would expect that on average immigrants would be older at the time of first treatment in high than low ethnic density neighborhoods. If immigrants were more likely to be repatriated to the country of origin in high than low ethnic density neighborhoods, we would expect to observe a stronger ethnic density interaction in first-generation than in second-generation immigrants (first-generation immigrants are more likely to be repatriated). We evaluated these predictions in our data.

Results

During the study period, 91 Moroccan, 94 Surinamese, 55 Turkish and 226 native Dutch subjects made first contact with a physician for a psychotic disorder. Table 4.2 shows the sociodemographic characteristics and DSM IV diagnoses of the subjects. Three patients were homeless and thus could not be assigned to a particular neighborhood. Four hundred sixty three patients remained for analysis.

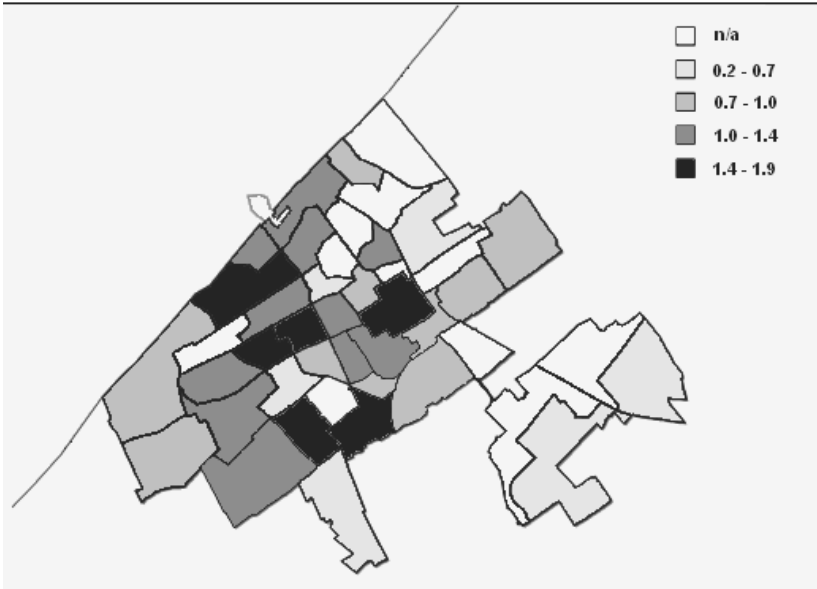


Figure 4.2 Standardized incidence ratios of psychotic disorders in total study population^a, across neighborhoods.

^a Ratio of observed versus expected cases, based on incidence rates indirectly standardized to age, sex, marital status and ethnic minorities in total study population, 1.0 is rate in standard population, n/a indicates no cases observed.

The incidence of psychotic disorders, adjusted for individual level age, sex, marital status, and non-Western ethnic minorities, varied from 0 to 64 per 100,000 person years across neighborhoods. The SIR of psychotic disorders across neighborhoods is shown in Figure 4.2.

The IRR of psychotic disorders for all immigrants together, compared to native Dutch, and adjusted for age, sex, marital status and neighborhood socioeconomic level, was

Table 4.3 Incidence rate ratios of first contact for psychotic disorders in different ethnic groups in The Hague, 1997-2005.

Ethnic group ^a	Cases	Person years	IRR ^b	95% CI
All immigrants	240	413586	2.22	1.78-2.76
Moroccans	91	88249	3.69	2.78-4.90
Surinamese	94	203088	1.88	1.45-2.44
Turks	55	122249	1.75	1.25-2.46
Native Dutch	226	1056172	1.0	

^a As defined in text, immigrant groups include first and second generation.

^b Fixed effect of individual ethnicity on incidence of psychotic disorders, in multi-level Poisson regression model, adjusted for age, sex, marital status and neighborhood socioeconomic level.

Table 4.4 Incidence rate ratios (IRR) of psychotic disorders in immigrants compared with native Dutch in The Hague, by neighborhood ethnic density, 1997–2005.^a

Ethnic group	Ethnicity stratified by ethnic density ^b			
	Low density		High density	
	IRR	95% CI	IRR	95% CI
All immigrants	2.36	1.89-2.95	1.25	0.66-2.37
Moroccans	4.43	3.28-5.97	1.56	0.75-3.21
Surinamese	1.88	1.42-2.50	1.19	0.58-2.44
Turks	1.74	1.16-2.60	1.12	0.55-2.30
Native Dutch	1.0		1.0	

^a All associations adjusted for age, sex, marital status and socioeconomic level of neighborhood.

^b Ethnicity effect sizes stratified as two highest ethnic density neighborhoods and other neighborhoods.

2.22 (95% CI, 1.78-2.76). The incidence rates were increased for all immigrant groups separately as well (Table 4.3).

In the stratified multi-level analysis of neighborhood ethnic density, the adjusted IRR (95% CI) was 2.36 (1.89-2.95) among immigrants living in neighborhoods with low density, and was 1.25 (0.66-2.37) among immigrants in high density neighborhoods. Also, for each separate immigrant group, the IRR was higher for immigrants living in low density neighborhoods (Table 4.4).

The multi-level Poisson regression model indicated a strong negative interaction between ethnicity at the individual level and the continuous measure of neighborhood ethnic density. The adjusted IRR of the interaction variable was below 1 for all immigrants together (adjusted IRR 0.95, $\chi^2 = 15.04$, $df = 1$, $p = 0.0001$) and for each immigrant group separately (Moroccans: IRR 0.93, $p = 0.002$; Surinamese: IRR 0.98, $p = 0.334$; Turks IRR 0.97, $p = 0.109$). This negative interaction can be interpreted to mean that psychosis incidence rates were more severely increased among immigrants in neighborhoods with a lower proportion of residents of the same ethnicity.

Additional analyses were undertaken to check for ascertainment bias. The mean age at first treatment contact was similar for immigrants in high and low ethnic density neighborhoods: 26.97 (sd, 7.37) and 26.24 (sd, 7.49) respectively ($t = 0.71$, $p = 0.48$). The difference in the adjusted IRRs for high versus low ethnic density neighborhoods was similar for first-generation immigrants (1.20 [95% CI, 0.62-2.34] versus 2.51 [1.95-3.23]) and second-generation immigrants (1.27 [0.61-2.64] versus 2.13 [1.53-2.97]).

Discussion

The increased incidence of psychotic disorders among immigrants in The Hague depended strongly upon neighborhood context. Compared to native Dutch, the incidence among immigrants increased when they lived in neighborhoods where their own ethnic group comprised a smaller proportion of the population. In low ethnic density neighborhoods, immigrants had a markedly increased incidence, whereas in high ethnic density neighborhoods, the incidence rate was not significantly higher than that of native Dutch.

Similar patterns were evident for Moroccan, Surinamese, and Turkish immigrant groups examined separately. The incidence rate of psychotic disorders was significantly increased only among immigrants living in low ethnic density neighborhoods (Table 4.4). The Moroccan group exhibited the highest incidence rates of psychotic disorders, and the difference between low and high ethnic density neighborhoods was largest for Moroccan immigrants.

The effect of ethnic density was not due to confounding by neighborhood deprivation. Neighborhood socioeconomic level was measured by municipal data and adjusted for in the analysis. Moreover, such confounding would tend to suppress the contribution of low ethnic density to psychosis among immigrants, because the most deprived neighborhoods had the highest concentration of immigrants (see Figure 4.1 and Table 4.1).

Previous findings

Our results are consistent with those from the seminal ecological study of Faris and Dunham during the 1930s in Chicago, which found higher hospital admission rates for schizophrenia among African Americans living in predominantly white neighborhoods ⁷, and, as noted earlier, extend the findings of Boydell and colleagues in London, who reported a “dose-response” relation with increasing incidence of schizophrenia in ethnic minorities as the proportion of such minorities in an area fell ⁸. The London study used appropriate multi-level statistical techniques, and investigated treated incidence rates rather than hospital admission rates. Cases were identified by studying case records of a past ten-year period. The association between ethnic density and schizophrenia could not be fully investigated in this study, however, as it was not possible to investigate differential case ascertainment across neighborhoods or prodromal drift to low ethnic density neighborhoods, and because information on ethnicity was limited. The ethnicity of cases had to be assessed by a description in the case notes, and population data were not precise enough to study ethnic minority groups separately. Comparisons could be made between a “white” group and a “non-white” group. The latter group consisted

largely of ethnic groups that may describe themselves as Black British, but although it may be hypothesized that such a shared identity is relevant to the ethnic density effect, there are many social, demographic, economic and cultural differences among these ethnic groups. Finally, a recent study reported an association between ethnic fragmentation and the incidence of schizophrenia, and found some evidence for an ethnic density effect, as the risk of schizophrenia was highest among ethnic minorities living in neighborhoods with the lowest ethnic density¹⁷.

Building upon these studies, we used a prospective incidence study involving first contact with both secondary and primary health care services. We were able to assess the confounding effect of marital status¹⁸, and to conduct additional analyses to investigate alternative explanations for the findings. Moreover, we had obtained population data that enabled us to calculate ethnic density as the proportion of one's *own* ethnic group in the neighborhood. This approach takes the heterogeneity of ethnic minorities into account, and allowed us to study each ethnic group separately.

Strengths and limitations

This study was large enough to examine neighborhood variation in the incidence of psychotic disorders for several immigrant groups within a single urban area. The numbers of cases in both low and high ethnic density neighborhoods were sufficient to test interactions between individual ethnicity and neighborhood ethnic density in a multi-level analysis. The numerators of the incidence rates were reliable, since the incident cases were derived from all sources of treatment in a defined geographical area and were assessed with a rigorous diagnostic protocol.

The denominators of the incidence rates were reliable. The person-years were not derived from a census, but from a comprehensive, continuously updated municipal registration system. Registration with municipal authorities is compulsory for all individuals residing legally in the Netherlands and a prerequisite for obtaining essential documents and possible aid (e.g. income support). The data from a recent report on illegal foreigners in the Netherlands¹⁹ suggest that the number of Moroccan, Surinamese and Turkish immigrants staying illegally in The Hague is less than 2000. Thus, under-enumeration of ethnic minorities is unlikely to explain the findings.

We were able to adjust for single marital status, which has been associated with higher rates of schizophrenia, particularly in neighborhoods with fewer single-person households¹⁸. The results remained statistically significant, indicating that the ethnic density effect cannot be attributed to greater probability of single marital status among individuals living in low ethnic density neighborhoods.

A limitation of the study may be that all psychotic disorders were included in the analysis rather than only schizophrenia. However, this approach minimized the potential for diagnostic bias. It has been suggested that immigrant patients with affective psychosis may present with more severe psychotic symptoms than non-immigrant patients, which may lead to misclassification of affective psychosis as schizophrenia²⁰. In addition, many investigators argue that the validity of psychotic disorders as a group may be greater than that of the restricted group of schizophrenia, which is a diagnosis of uncertain validity²¹. When the sample was restricted to schizophrenia spectrum disorders, similar results were found (adjusted IRR ethnic density interaction all immigrants = 0.96, $\chi^2 = 6.36$, $df=1$, $p = 0.012$).

In the stratified analysis, we classified two neighborhoods with large immigrant populations as high density and the other 42 neighborhoods as low density. Since the threshold for the ethnic density effect is not known, other stratifications may be more valid. When we used alternative approaches to stratify ethnic density, the results were similar (available from first author).

Neighborhood ethnic density was assessed and investigated at the time of first treatment contact. In future studies, it might be feasible to collect longitudinal data on neighborhood context in childhood and adolescence. This approach could be used to verify that exposure to a low ethnic density neighborhood is antecedent to the onset of psychotic symptoms, and to determine the developmental period during which neighborhood ethnic density is most important.

Socioeconomic status of the family of origin could not be adjusted for. Previous studies have found variable and modest associations of low family socioeconomic status and incidence of psychotic disorders^{22,23}. In addition, it is difficult to see how low ethnic density would be related consistently to low individual socioeconomic status, because neighborhoods with the highest proportion of non-Western immigrants are deprived to a level not paralleled anywhere in the primarily Dutch neighborhoods.

A paramount concern in the interpretation of these results is the potential for differences in case ascertainment between low and high ethnic density neighborhoods. If immigrants who are clustered together in high density neighborhoods are less likely to use Dutch health services when they develop psychotic symptoms, this could produce an artifactual ethnic density effect. For several reasons, however, this potential ascertainment bias is unlikely to account for our findings. Health insurance is compulsory for all individuals residing legally in the Netherlands, and immigrants visit their general practitioners more often than native Dutch do²⁴. Ascertainment in this study was an integral part of an early psychosis treatment program, which entailed active collaboration with

general practitioners throughout the city. Furthermore, additional analyses conducted to detect such ascertainment bias were reassuring. Immigrants ascertained in low and high ethnic density neighborhoods were similar in age of onset; and the variation in rates between low and high ethnic density neighborhoods pertained to both first- and second-generation immigrants.

The results could reflect a process of social selection rather than social causation. It is conceivable that individuals with psychotic disorders moved from high to low density neighborhoods prior to their first treatment contact, perhaps during the prodromal period of their illness. However, the mean proportion of own ethnic group in the neighborhood did not differ significantly between the immigrant cases who still lived with their parents (35% of the cases) and those who did not (mean density 11.62% and 10.68% respectively, $t = -0.82$, $p = 0.41$). Thus, there is no evidence that patients who had already left the parental home selected neighborhoods of residence with a lower ethnic density. One might still speculate that the parents of the immigrants who developed psychotic disorders had previously moved from high to low ethnic density neighborhoods as a result of these parents' genetic predisposition to psychosis. However, genetic risk for psychosis is not associated with upward social mobility²⁵. In The Hague, moving from a high to a low ethnic density neighborhood generally means moving to a neighborhood with a higher socioeconomic level.

Implications

The most plausible interpretation is that our measure of neighborhood ethnic density captured a social experience that had a quantifiable impact on the incidence of psychotic disorders. Animal and human studies also indicate that social experiences can affect brain development and the risk of mental disorders^{26,27}. At present, we can only speculate how the particular social experiences of immigrants could influence the emergence of psychoses. The finding of a similar ethnic density effect among first- and second-generation immigrants implies that ethnic density represents social experiences which are relevant for both generations.

Several mechanisms may be considered, which are not mutually exclusive. One possibility is that high ethnic density mitigates the pathogenic effects of discrimination^{8,28}. We have reported elsewhere that the increased risk of schizophrenia for non-Western ethnic minority groups was associated with the ethnic minority groups' experiences of discrimination²⁹, and some studies have found that perceived discrimination may foster the emergence of psychotic symptoms^{30,31}. Conceivably, living in a high ethnic density neighborhood could buffer the impact of discrimination and stigma^{32,33} by enhancing

positive identification with one's own ethnic group, or could reduce exposure to discrimination by reducing daily contact with the native Dutch majority.

Another possibility is that high ethnic density, which is likely to be associated with greater probability of social support, increases access to normalizing explanations for anomalous perceptual experiences and abnormal beliefs, that are present in individuals at high risk for developing psychosis³⁴. Whereas social isolation may contribute to the acceptance of a psychotic appraisal of these early abnormal mental states, a social network may have a normalizing function, thus preventing transition into psychosis³⁵.

Conclusion

The relationship between immigration and psychosis in Western Europe is a major public health concern, but still not understood. These data suggest that this relationship depends in part upon the neighborhood characteristic of ethnic density. The findings also have broader implications in suggesting that social context can play an important role in the etiology of schizophrenia and other psychotic disorders.

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5

Discrimination and the incidence of psychotic disorders among ethnic minorities in the Netherlands

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Abstract

Background: It is well established now that the incidence of schizophrenia is extremely high for several ethnic minority groups in western Europe, but there is considerable variation among groups. We investigated whether the increased risk among these groups depends upon the degree to which they perceive discrimination based on race or ethnicity.

Methods: We studied the incidence of psychotic disorders over seven years in The Hague, a city with a large and diverse population of ethnic minorities. To compare the incidence of schizophrenic disorders (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) in each ethnic minority group with the incidence in native Dutch, we computed incidence rate ratios (IRRs). Based on a population study and on rates of reported incidents of discrimination in The Hague, the degree of perceived discrimination of ethnic minority groups was rated: high (Morocco), medium (Netherlands-Antilles, Surinam and 'other non-Western countries'), low (Turkey), or very low ('Western or westernized countries').

Results: The age- and gender-adjusted IRRs of schizophrenic disorders for ethnic minority groups exposed to high, medium, low and very low discrimination were 4.00 (95% CI 3.00-5.35), 1.99 (1.58-2.51), 1.58 (1.10-2.27) and 1.20 (0.81-1.90) respectively. When not only schizophrenic, but all psychotic disorders were included in the analysis, the results were similar.

Conclusions: These results suggest that discrimination perceived by ethnic minority groups in western Europe, or some factor closely related to it, may contribute to their increased risk of schizophrenia.

Introduction

The incidence of schizophrenia and other psychotic disorders is very high in several ethnic minority groups in western Europe ^{1,2}. A broad spectrum of ethnic groups is affected, but there is considerable heterogeneity across groups ³. In the UK, the risk for African-Caribbeans is much higher than for South Asians ², and in the Netherlands, the risk for immigrants from Morocco is higher than for those from Turkey ¹. While these findings may offer clues to the etiology of psychotic disorders, thus far they have defied explanation ⁴. As the excess cannot be explained by any known bias or biological risk factor ³, investigators have turned attention to the possible role of the social context in which ethnic minorities live ⁵. Measured variation across groups in aspects of the social context can be used to find out which factors may contribute to the observed variation in the incidence of schizophrenia ⁶.

Discrimination based on ethnic background, skin color or race (hereafter referred to as discrimination) has been suggested as one such factor ^{3,4}. Discrimination has many facets, which tend to be correlated and difficult to disentangle. It comes in interpersonal experiences of racist insults or violence, but also in structural discrimination by institutions, as in employment policies or access to education or housing facilities. Discrimination may be directed at individuals or at groups, it can be found in opinions, attitudes and in behaviors, may be measured by objective events or by subjective perceptions of events ^{7,8} and has a pervasive, adverse influence on health of ethnic minority populations ⁹.

Some cross-sectional studies have reported an association between perceived discrimination and the prevalence of psychosis at the individual level ^{10,11}, and a prospective study in the Netherlands suggested that perceived discrimination (albeit not only racial, but any discrimination) may induce the onset of delusional ideations ¹². A recent meta-analysis of incidence studies of psychotic disorders found that the risks were particularly high for dark-skinned immigrants, who are likely to experience a higher degree of discrimination ³. Perceived discrimination may be an important determinant of psychotic disorders not only at individual level, but also at group level. Ethnic minority groups differ in terms of their stigmatized status in society. Members of these groups develop shared understandings of this status, which include knowledge of negative cultural stereotypes of their identity, awareness that they are devalued in the eyes of others and recognition that they could be victims of discrimination ¹³⁻¹⁵. Independent of personal experiences, these collective representations of stigma have been associated with poor health outcomes ^{15,16}.

In the present study, we examined the association between perceived discrimination as a group characteristic and the incidence of psychotic disorders in ethnic minorities. We used data from a first-contact incidence study of psychotic disorders over seven years, conducted in the city of The Hague, a city with a large and diverse population of ethnic minorities. We hypothesized that the incidence in ethnic minorities is associated with the extent to which these groups perceive discrimination.

Methods

Classification of ethnicity

The municipality of The Hague keeps records of citizens' country of birth and that of their parents. In this study, we used the classification of ethnicity as defined by the Netherlands' Bureau of Statistics. Dutch ethnicity is assigned to citizens who are Dutch-born and whose parents were also born in the Netherlands (hereafter referred to as native Dutch). If a citizen, or (one of) his or her parents, was born abroad, he or she is assigned to the group of people born in the same country. If the parents were born in different foreign countries, the country of birth of the mother determines the assignment to a particular group. Since they share the background of their country of origin, immigrants and their children are assigned to the same group. Foreign countries of birth are condensed into six categories: 1. Morocco, 2. Surinam, 3. Netherlands Antilles, 4. Turkey, 5. Western or westernized countries (northern, southern or western Europe, the former Yugoslavia, the USA, Canada, Australia, New Zealand, Japan or former Netherlands East Indies), 6. All other (non-Western) countries. On January 1, 2005, The Hague had 472,087 inhabitants, of whom 45.2 % was born outside the Netherlands or had a parent born outside the Netherlands.

Ratings of discrimination

Two independent sources were used to rate ethnic minority groups on perception of discrimination.

First, a population study¹⁷ measured personal experiences of discrimination among a sample (N = 459) of people from non-Western ethnic minorities in five cities in the Netherlands, including The Hague (N=100). The participants were recruited in public areas, such as markets, mosques, community centers, shops and on the street. They were on average very similar to their respective ethnic groups in the Netherlands in terms of age, sex, generation, religion and unemployment rate, but had somewhat higher levels of education. Participants were interviewed in spring 2001, by research assistants who were matched with participants on ethnicity. Table 5.1 shows results for the question

Table 5.1 Rates of perceived interpersonal discrimination in five cities in the Netherlands in 2001, per ethnic group.

Ethnic group ^a	Experiences of interpersonal discrimination ^b	Category
Morocco	42 %	High
Netherlands Antilles	30 %	Medium
Surinam	26 %	
Other non-Western	24 %	
Turkey	8 %	Low

^a As defined in text, first- and second-generation included.

^b Proportion of ethnic minorities that reported any interpersonal experience of discrimination in last year, population survey, 2001 (N=459)¹⁷.

about whether respondents had experienced incidents of interpersonal discrimination within the last year, dichotomized as: no experience, and any experience of a racist insult, threat, or violence.

Second, complaints and reports of discrimination based on ethnic background, skin color, race or religion, are collected in The Hague by the Anti Discrimination Bureau¹⁸. This bureau actively monitors the nature and degree of discrimination in The Hague and offers support to those who report any incident of discrimination. Table 5.2 shows the numbers of reports per ethnic group over the years 2001-2005. Incidents involved unequal or hostile treatment, insults, threats and violence, in a context ranging from the labor market, restaurants, media, access to housing and education, to perceived discrimination by police, passers-by on the street or neighbors. We calculated rates of the ethnic groups' perceived discrimination by dividing the absolute numbers of reported incidents as published in the report¹⁸ by the number of person-years.

Based on both measures, we rated the ethnic groups according to degree of perceived discrimination. In case of discrepancy between the two sources, we used the results of

Table 5.2 Rates of reported incidents of discrimination in The Hague, 2001-2005, per ethnic group.

Ethnic group ^a	Person years ^b	Number of incidents of discrimination ^c	Rate ^d	Category
Morocco	112,298	230	204.8	High
Other non-Western countries	224,241	373	166.3	Medium
Netherlands Antilles	52,422	70	133.5	
Surinam	221,188	176	79.6	
Turkey	147,447	97	65.8	Low
Western countries	251,487	56	22.3	Very low

^a As defined in text, first- and second-generation included.

^b Population 2001-2005.

^c Absolute numbers of complaints and reports of discrimination, 2001-2005, Anti Discrimination Bureau The Hague¹⁸.

^d Per 100,000 person-years.

the population survey as the primary measure, because we regarded the second source as a less accurate measure of discrimination, as it involves not only the perception of discrimination, but also the step to report these perceptions to an Anti Discrimination Bureau. In fact, the results from the two measures were remarkably concordant, except that Surinamese scored higher in the population survey than in the municipal data.

Thus, we rated the ethnic groups as perceiving high (Morocco), medium (Netherlands Antilles, Surinam, other non-Western countries), low (Turkey), or very low (Western or westernized countries) discrimination (Tables 5.1 and 5.2).

Neighborhood deprivation

Neighborhood deprivation, defined by high proportions of unemployed persons, low average income, poor quality of housing and high crime rates, negatively influences health¹⁹ and has been associated with high rates of schizophrenia in some studies²⁰. Therefore, investigations of the social context should take neighborhood deprivation into account. The Hague consists of 44 neighborhoods. A measure of the socioeconomic level of the neighborhoods was provided by the municipality. This score is based on proportion long-term unemployed, mean income, quality of housing, and mean level of education (but not proportion of ethnic minorities). The average socioeconomic level of the city has been set as zero; scores of the neighborhoods ranged from -21.8 to 26.9. The most deprived neighborhoods were located in the city center.

Incidence of psychotic disorders

Subjects

The study was conducted in two phases (April 1, 1997 - April 1, 1999 and October 1, 2000 - October 1, 2005). Previous reports have detailed the methods of this study and presented descriptive data on incidence rates up to 2002^{1,21}. Briefly, the criteria for inclusion and exclusion were similar to those used in the World Health Organization Ten-Country study²². There was collaboration with the local general practitioners, psychiatrists and residents in psychiatry, to get access to every possible case. Over the seven years of the study, 678 citizens of The Hague aged 15-54 years made first contact with a physician for a (suspected) psychotic disorder. Diagnostic interviews were conducted by the research team in 497 cases (73 %) and interviews with relatives in 420 cases (62%). For the patients who refused to be interviewed, the physicians provided detailed clinical information. Differences in the proportions of refusers across the discrimination categories were small (29%, 25%, 25% and 26% for very low, low, medium and high discrimination respectively).

Of the total of 678 patients, 60 were excluded on the basis of being diagnosed with a substance-induced psychotic disorder, a psychotic disorder due to a somatic condition or a non-psychotic disorder, using the diagnostic protocol described below.

Except in the first two years, when the protocol was used primarily for research purposes²¹, patients were being identified for inclusion in an early psychosis treatment service. The study was approved by the ethics committee of University Medical Center Utrecht.

Diagnostic protocol

The patients were interviewed by Dutch residents in psychiatry, using the Dutch translation of a semi-structured diagnostic interview, the Comprehensive Assessment of Symptoms and History (CASH)²³. Relatives were interviewed by trained nurses, using the Instrument for the Retrospective Assessment of the Onset of Schizophrenia (IRAOS)²⁴. If necessary, an official interpreter was available to help in the administration of the CASH or IRAOS. In addition, the residents asked the physicians of the patients for detailed clinical information. Based on CASH, IRAOS and clinical information, the residents compiled a narrative history of the patient's illness. For the patients who had refused to participate in the interviews, a history was made with the anonymised clinical information. During a diagnostic meeting, two psychiatrists made a consensus DSM IV diagnosis on the basis of the narrative history.

Statistical procedures

The municipality of The Hague provided population figures per country of birth, gender, five-year age-group and neighborhood for the years of the study, yielding 1,870,408 person-years of observation. First-contact rates were calculated by dividing the number of cases by the number of person-years (ages 15 to 54). Incidence rate ratios (IRR) and 95% confidence intervals (95% CI) were calculated by Poisson regression analysis, using the STATA statistical program, 9.0 version.

All comparisons of ethnic minority groups with native Dutch were adjusted for five-year age-group, gender and socioeconomic level of the neighborhood. The effects of discrimination were tested for statistical significance by Wald tests²⁵.

Additional analyses were conducted to address diagnostic bias. A potential source of bias in this study is overdiagnosis of schizophrenic disorders (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) among people from ethnic minorities presenting with psychotic symptoms²⁶. Therefore we also examined the effects of discrimination for the incidence of all psychotic disorders. In addition, in the first phase (1997-1999), the psychiatrists who made the diagnosis were blinded for ethnicity by omitting any clue to a patient's ethnicity in the narrative history, to ensure that their

Table 5.3 Sociodemographic variables and diagnoses of the cases identified in the study.

Number of participants	618
Male gender, No. (%)	436 (70.6)
Mean age (SD)	
Male	26.6 (7.8)
Female	29.3 (8.7)
Ethnicity, No. ^a	
Morocco	91
Surinam	94
Netherlands Antilles	21
Turkey	55
Other non-Western countries	97
Western countries	34
Native Dutch	226
Diagnosis, No.	
Schizophrenic disorder ^b	424
Major depressive disorder with psychotic features	25
Bipolar disorder with psychotic features	38
Delusional disorder	10
Brief psychotic disorder	33
Psychotic disorder, not otherwise specified	88

^a As defined in text, includes first and second generation.

^b Includes DSM IV categories schizophrenia, schizophreniform disorder, and schizoaffective disorder.

perceptions of ethnic minorities could not influence their diagnoses. In the second phase (2000-2005), all relevant information about a patient's ethnicity was included. The proportions of patients from non-Western ethnic minorities that received a diagnosis of a schizophrenic disorder were compared between the two diagnostic methods.

Results

Of the 436 men and 182 women who made first contact for a psychotic disorder, 311 men and 113 women were diagnosed with a schizophrenic disorder. The overall first-contact rate for schizophrenic disorders was 33 (95%, CI 30-36) per 100,000 person-years. Table 5.3 shows the demographic characteristics and diagnoses of the cases identified in the study.

Across ethnic minority groups, the incidence of schizophrenic disorders increased with degree of perceived discrimination. Compared with native Dutch, the IRRs among ethnic minority groups, adjusted for age and sex, were 4.00 (95% CI 3.00-5.35), 1.99 (1.58-2.51),

Table 5.4 Incidence rate ratios (IRRs) for schizophrenic disorders ^a by degree of perceived discrimination and ethnic group.

Degree of discrimination ^d Ethnic group	Cases / Person- years	Unadjusted		Adjusted ^b		Adjusted ^c	
		IRR	95% CI	IRR	95% CI	IRR	95% CI
High							
Morocco	70 / 88249	5.90	4.43-7.85	4.00	3.00-5.35	3.52	2.56-4.83
Medium							
Netherlands Antilles	13 / 45064	2.46	1.95-3.09	1.99	1.58-2.51	1.84	1.44-2.36
Surinam	72 / 203088	2.15	1.22-3.79	1.64	0.93-2.90	1.54	0.87-2.74
Other non-Western countries	65 / 205697	2.64	1.99-3.50	2.21	1.66-2.94	2.05	1.52-2.77
Low							
Turkey	37 / 122249	2.35	1.75-3.15	1.87	1.39-2.51	1.73	1.28-2.35
Very low							
Western countries	25 / 149889	1.24	0.81-1.90	1.20	0.79-1.84	1.17	0.76-1.81
Native Dutch	142 / 1056172	1.00		1.00		1.00	

^a Includes DSM IV categories schizophrenia, schizophreniform disorder, and schizoaffective disorder.

^b Adjusted for age and gender.

^c Adjusted for age, gender and socioeconomic level of the neighborhood.

^d As defined in text.

1.58 (1.10-2.27) and 1.20 (0.79-1.84) for high, medium, low and very low degree of discrimination respectively (Table 5.4). In this Poisson regression model, the adjusted pooled χ^2 for degree of discrimination was 95.97, $df=4$, $p < 0.0005$. Table 5.4 also gives the IRRs for the separate ethnic minority groups.

Further adjustment for socioeconomic level of the neighborhood slightly attenuated the effects of discrimination, particularly in the groups exposed to the most discrimination (Table 5.4).

Table 5.5 Incidence rate ratios (IRRs) for all psychotic disorders by degree of perceived discrimination.

Degree of discrimination ^c	Cases / Person-years	Unadjusted		Adjusted ^a		Adjusted ^b	
		IRR	95% CI	IRR	95% CI	IRR	95% CI
High	91 / 88249	4.82	3.78-6.15	3.50	2.73-4.47	3.00	2.30-3.93
Medium	212 / 453849	2.18	1.81-2.63	1.84	1.52-2.22	1.68	1.37-2.05
Low	55 / 122249	2.10	1.57-2.82	1.56	1.16-2.10	1.36	0.99-1.86
Very low	34 / 149889	1.06	0.74-1.52	1.03	0.72-1.48	1.01	0.70-1.46
Native Dutch	226 / 1056172	1.00		1.00		1.00	

^a Adjusted for age and gender.

^b Adjusted for age, gender and socioeconomic level of the neighborhood.

^c As defined in text.

Additional analyses were conducted to check for diagnostic bias. When the analysis was extended to include all psychotic disorders, the results were similar (Table 5.5). The proportion of patients from non-Western ethnic minorities that received a diagnosis of a schizophrenic disorder was 65 % (70/108) in the first phase and 75 % (186/249) in the second phase ($\chi^2 = 3.63$, $df = 1$, $p = 0.06$).

Discussion

The increased risk of schizophrenia and other psychotic disorders for ethnic minority groups in western Europe is a consistent and strong finding³, which thus far has defied explanation. It is also evident that the degree of increased risk of schizophrenia varies substantially among these ethnic minority groups. The results of the present study in The Hague may take us a step toward understanding this phenomenon. The incidence of psychotic disorders varied across ethnic minority groups by degree of perceived discrimination: the incidence was higher when groups perceived more discrimination.

Our data suggest that belonging to an ethnic minority group perceiving a high degree of discrimination is a risk factor for psychotic disorders, rather than immigration per se. We measured discrimination as a group level characteristic, shared by all the members of the group. Belonging to a group that is stigmatized or discriminated against, has been linked to poor mental health, physical illness, and academic underachievement⁹, not only in individuals who perceive direct interpersonal discrimination, but also in those who experience that their group is discriminated against and stigmatized^{16,27}. Perceptions and impact of discrimination appear to be influenced by group characteristics such as ethnic support, collective self-esteem^{13,15,28} and perhaps also sensitivity for discrimination. It should nonetheless be emphasized that the effect of a group level factor does not preclude individual variation in experience which also influences disease risk. Within an ethnic group individual perceptions of discrimination vary, and influence disease risk.

The findings are consistent with studies from the United Kingdom. The highest risk of psychotic disorders has been found in the African-Caribbean population², which is the ethnic minority group that also reported the highest degree of discrimination¹¹.

Our rating of discrimination for ethnic minority groups was based on measures of perceived discrimination, but discrimination is also present in structural, institutional forms⁸, or in prejudiced attitudes of the majority population⁷. The Moroccan population in the Netherlands probably has the highest ratings on all these dimensions of discrimination.

The Moroccan ethnic group had the highest rating on perceived discrimination in this study, has the highest unemployment rate of all ethnic minority groups and is disliked most by native Dutch²⁹. However, these dimensions are not necessarily concordant for other ethnic groups. The Turkish group has only a slightly better socioeconomic position than the Moroccan group, and yet is rated low in terms of perceived discrimination. The Surinamese and Antillean groups are liked better than the Turkish group by the native Dutch and are less often unemployed²⁹, and yet are rated higher in terms of perceived discrimination. Thus, perception of discrimination may be an important factor in the relationship between discrimination and psychosis, even when taking into account structural discrimination or socioeconomic consequences of discrimination. This is consistent with our finding that the effects of perceived discrimination did not change significantly after adjustment for socioeconomic level of the neighborhood, and with recently developed conceptual models that explicitly place racial discrimination within a stress framework and focus on perceived racism as an important determinant of health⁷.

An important next step for understanding etiology is to determine the mechanism by which groups' perceptions of discrimination would result in individuals developing schizophrenia, a neurodevelopmental disorder. The profoundly difficult and inescapable experience of ongoing discrimination and stigma may present a threat to social identity of individuals, which is a severe cognitive and emotional challenge¹⁵. Individuals with a genetic vulnerability to schizophrenia often have impaired executive function³⁰, and when subjected to such a severe challenge, they may be more likely to develop the disorder³¹. This may apply in particular to those who have a greater tendency for making external attributions, as these attributions may lead to paranoid ideations and in extreme form to persecutory delusions^{32,33}. Animal experiments are of some relevance here. In male rats, repeated exposure to social defeat leads to sensitization of the mesolimbic dopamine system, i.e., an enhanced behavioral and dopamine response to dopamine agonists³⁴. The mesolimbic dopamine system of untreated schizophrenia patients has been demonstrated to be sensitized too³⁵. Consequently, if the results of the animal experiments can be extended to humans, it is possible that chronic exposure to discrimination, or other forms of social defeat, leads to disturbances in dopamine function and further the development of psychosis¹⁴.

Strengths and limitations

A major strength of this study is its size. Second, both the numerators (cases) and denominators (person-years) of the incidence rates were reliable. The incident cases were derived from all sources of treatment in a defined municipality and were assessed with a rigorous diagnostic protocol. The person-years were derived from a comprehensive mu-

nicipal registration system. Registration with municipal authorities is compulsory for all individuals residing legally in the Netherlands and a prerequisite for obtaining essential documents and possible aid (e.g. income support). The data from a recent report in the Netherlands³⁶ suggest that the number of illegal foreigners in The Hague is less than 7000. Thus, under-enumeration of ethnic minorities is unlikely to explain the findings.

We used two independent sources to rate ethnic groups on perceived discrimination^{17,18}. Both studies used different methods: one used interviews, the other relied on reported incidents of discrimination. The similar results of both measures argues for the validity of the rating of perceived discrimination in the years of the study. Nevertheless, based on the figures from the Anti Discrimination Bureau in The Hague alone (Table 5.2), it could be argued that Surinamese, who were assigned to the medium discrimination category, should be classified as experiencing low degree of discrimination. When we did so, the main effect of discrimination remained highly significant, but the difference in risk for the medium and low discrimination categories disappeared (results not shown).

Limitations of the study may include the system of classification of ethnicity. In the Netherlands, ethnicity is generally not determined by self-ascription, but by (parents') country of origin. However, this classification reflects the dominant consensus about ethnic categories in the Netherlands, which is relevant for group level discrimination and stigma, regardless of individual identification with these categories.

There may have been some misclassification of perceived discrimination of ethnic minority groups. Those from Western or westernized countries were all designated as perceiving low degree of discrimination. People from countries such as former Yugoslavia and Japan were assigned to the group of Western countries, but may differ from the majority population in skin color or behavior, and may experience discrimination to a higher degree. However, such misclassification could not have appreciably affected our results. These are small groups in The Hague, and we found only one case among them.

Diagnostic bias could have contributed to higher rates of schizophrenic disorder in groups that are discriminated against. Additional analyses addressed this potential bias. First, the results were similar when all psychotic disorders were included in the analyses rather than only schizophrenic disorder. Second, the proportion of non-Western patients receiving a diagnosis of schizophrenic disorder was slightly higher in the diagnostic protocol where the psychiatrists were not blinded for ethnicity compared to the protocol where they were blinded, but this difference was not statistically significant and too small to explain the findings.

Potential confounding

Socioeconomic status of the ethnic minority groups was not adjusted for. As noted earlier, this cannot fully account for our findings, because socioeconomic status is not highly concordant with perceived discrimination among these ethnic groups. For example, the risk of schizophrenia is lower for people with Turkish background than for Surinamese, but their socioeconomic status as a group is much lower than that of Surinamese²⁹.

We adjusted for neighborhood deprivation, but other neighborhood characteristics may also be important for the incidence of psychotic disorders. First, urban birth and upbringing is an established risk factor for schizophrenia³⁷. It is unlikely that this could explain differences in rates across ethnic minority groups, because the study was restricted to the urban population of The Hague. Prior history of residences may also influence the risk of later schizophrenia³⁷, but the majority of the second generation of all ethnic minority groups is born in The Hague and the large majority of first-generation immigrants from both Morocco and Turkey comes from rural areas, whereas the risk of schizophrenic disorder was much higher for Moroccans than for Turks¹.

Second, a low proportion of ethnic minorities living in the neighborhood has been associated with higher incidence of schizophrenia among these minorities⁵. Low ethnic density is likely to be associated with smaller probability of social support, which may lead both to higher degree of perceived discrimination and the onset of psychotic disorder. On the other hand, the ethnic density effect is often attributed to more exposure to or increased perception of discrimination among members of ethnic minority groups living in neighborhoods with low ethnic density³⁸. In that case, low ethnic density is not a confounding factor in the present study, but may be regarded as an antecedent or an indicator of perceived discrimination.

Use of cannabis is related to the onset of schizophrenia³⁹ and may be cause or consequence of discrimination. In the Netherlands, however, there is no clear evidence that the prevalence of drug use is higher in ethnic minority groups than among the majority population⁴⁰. Also, there was no association between ethnicity and drug use among cases in the first phase of our study⁴¹.

A long period of separation from parents in childhood has been associated with the incidence of schizophrenia, particularly among African-Caribbeans in the UK⁴². Prenatal exposures such as infection and nutritional deficiency have been related to the risk of schizophrenia^{43,44}. High paternal age at birth is a risk factor for schizophrenia in offspring⁴⁵. To account for our findings, these factors would have to be very strongly correlated with the degree of perceived discrimination across ethnic minority groups.

Conclusion

In these data, degree of ethnic groups' perceived discrimination was associated with the incidence of schizophrenia. Discrimination, or some factor that is strongly associated with discrimination, may be part of the explanation of an increased incidence among ethnic minorities in western Europe. This finding also underscores the importance of investigating discrimination as a determinant of health in minority populations.

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6

Perceived discrimination and the risk for schizophrenia in ethnic minorities: a case-control study

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Abstract

Background: Previous studies have reported a very high incidence of schizophrenia for immigrant ethnic groups in Western Europe. The explanation of these findings is unknown, but is likely to involve social stress inherent to the migrant condition. A previous study reported that the incidence of schizophrenia in ethnic groups was higher when these groups perceived more discrimination. We conducted a case-control study of first-episode schizophrenia, and investigated whether perceived discrimination at the individual level is a risk factor for schizophrenia.

Methods: Cases included all non-Western immigrants who made first contact with a physician for a psychotic disorder in The Hague, the Netherlands, between October 2000 and July 2005, and received a diagnosis of a schizophrenia spectrum disorder (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) (N=100). Two matched control groups were recruited, one among immigrants who made contact with non-psychiatric secondary health care services (N=100), and one among siblings of the cases (N=63). Perceived discrimination in the year before illness onset was measured with structured interviews, assessing experiences of prejudice, racist insults or attacks, and perception of discrimination against one's ethnic group. Conditional logistic regression analyses were used to predict schizophrenia as a function of perceived discrimination.

Results: Cases reported somewhat higher rates of perceived discrimination in the year prior to illness onset than their siblings and the general hospital controls, but these differences were not statistically significant; 52 percent of the cases and 42 percent of both control groups had perceived any discrimination. Perceived discrimination at the individual level was not a risk factor for schizophrenia in these data. Perceived discrimination was positively correlated with cultural distance and cannabis use, and negatively with ethnic identity, self-esteem, and mastery.

Conclusions: The relationship between racial discrimination and psychosis may vary with the aspect of discrimination that is studied, and may also depend upon the social context in which discrimination takes place.

Introduction

The incidence of schizophrenia and other psychotic disorders is very high among ethnic minority groups in western Europe ^{1,2}. Racial discrimination has been suggested as a possible explanation for this increased incidence ^{3,4}, but although many studies have shown that discrimination has a pervasive, adverse influence on health of ethnic minority populations ⁵, the relationship between discrimination and mental health is poorly understood ⁶, and research of the association between discrimination and psychosis is scarce ⁷. Two cross-sectional studies found an association between perceived discrimination and the prevalence of psychotic symptoms ^{8,9}, and a prospective study in the Netherlands suggested that perceived discrimination (albeit not only racial, but any discrimination) may induce the onset of delusional ideations ¹⁰. We have previously reported that the incidence of psychotic disorders in The Hague, the Netherlands, varied across ethnic minority groups by degree of perceived discrimination: the incidence was higher when groups perceived more discrimination ¹¹. Within an ethnic group, however, individual perceptions of discrimination vary, and may influence disease risk. These individual variations may depend upon many factors, including gender, educational level, generation, cultural distance, ethnic density, social support, self-esteem, and ethnic identity ^{5,12,13}.

We are not aware of any published research on discrimination as risk factor for schizophrenia at the individual level. The present case-control study of first episode schizophrenia among ethnic minorities in The Hague aimed to investigate the association between perceived discrimination and schizophrenia, and to explore factors that influence degree of perceived discrimination at the individual level.

Methods

Classification of ethnicity

We used the classification of ethnicity as defined by the Netherlands' Bureau of Statistics. If a citizen, or (one of) his or her parents, was born abroad, he or she is assigned to the group of people born in the same country. If the parents were born in different foreign countries, the country of birth of the mother determines the assignment to a particular group.

Participants

Cases

All first- or second-generation immigrants from non-Western countries (of which 85% from Surinam, Morocco, Turkey, or Netherlands-Antilles), aged 18-54 years, who made first contact with a physician in The Hague for a psychotic disorder and received a diagnosis of a schizophrenia spectrum disorder (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) between October 1, 2000 and July 1, 2005, were eligible for the study. Case-finding procedures and diagnostic protocol of the study have been described elsewhere ². If the patient had been adopted as a child, he or she was excluded (N = 4).

Controls

For each patient, two control subjects were recruited, matched for five-year age-group, sex, and ethnicity (including generation). They were screened for psychotic symptoms (see Measures), and were excluded if these were present (N = 5).

The first control group was recruited among the general ethnic minority population of The Hague. To minimize selection bias as a result of pathways to care, the controls were selected from immigrants who made contact with non-psychiatric secondary health care services. Controls were recruited from the outpatient departments of Internal Medicine and Surgery of a general hospital. The reasons for making contact with these departments differed widely, and included: lipoma or naevus (N = 15), fracture (N = 8), contusion (N = 11), haemorrhoids (N = 8), sinus pilonidalis (N = 5), anal fissure (N = 5), inflammatory bowel disease (N = 5), diabetes mellitus (N = 5), and other, less frequent diagnoses (N = 38).

The second control group consisted of siblings of the patients, in order to (partially) control for genetic factors.

All participants gave written informed consent for the study. The study was approved by the local ethics committee. Structured interviews were conducted by a resident in psychiatry (WV) and four trained research assistants. If participants did not speak Dutch sufficiently (N = 9), trained research assistants (N = 3) who were native speakers in Turkish, Kurdish, Urdu, Arabic or Berber, conducted the interviews. Because we expected this in advance to concern only a small minority of the sample, we neither developed nor maintained a protocol for translation and back-translation of the questionnaires.

Participants were instructed to answer according to their experiences in the year before illness onset, the date of which was determined first.

Measures

Psychotic symptoms

In control subjects, the psychosis section of the Composite International Diagnostic Interview (CIDI), version 2.1¹⁴, was administered.

Perceived discrimination

This scale was developed by the International Comparative Study of Ethnocultural Youth (ICSEY)¹⁵, a study among more than 10,000 adolescents from 30 ethnic groups in 13 countries, which included Surinamese, Turkish and Antillean immigrants in the Netherlands. The scale is an ordinal measure; response options range from “strongly disagree” (1) to “strongly agree” (5). The scale consists of five items:

I think that others have behaved in an unfair or negative way towards my ethnic group;

I don't feel accepted by Dutch people;

I feel Dutch people have something against me;

I have been teased or insulted because of my ethnic background;

I have been threatened or attacked because of my ethnic background.

We used the total scale score as a measure of perceived discrimination. For further exploration, we also used item (1) as a separate measure of perceived discrimination against one's own group, and items (2) to (5) as perceived individual discrimination. Finally, for the total and for the exploratory measures, dichotomous variables were created. Responses of “Somewhat agree” or “Strongly agree” on any of the items were classified as “Yes”, all other scores as “No”.

Other measures

We assessed several sociodemographic and social factors that previously have been associated with perceived discrimination or schizophrenia, and may be considered as potential confounding or mediating factors in their relationship. Socioeconomic status was assessed with level of education (no or primary, secondary, or higher education) and employment status (unemployed or else). Information was noted on marital status (single or else) and on lifetime cannabis use (use defined as more than five times). Cultural distance was measured with 25 statements involving emancipation, autonomy and authority, secularization, and moral values (adapted from¹⁶). Ethnic density was calculated as the proportion of members of one's own ethnic group living in the neighbourhood. The required population data were provided by the municipal authorities¹³. Measures of ethnic identity and mastery were adapted from the International Comparative Study of Ethnocultural Youth (ICSEY)¹⁵. The scale of Ethnic Identity assesses ethnic affirmation and feelings about being a group member, the Mastery scale assesses locus of control¹⁵. We also used the 15-item Rosenberg Self-Esteem Scale¹⁷, and the 12-item Shortened

Social Support Scale¹⁸. In this paper, we address the associations of these measures with perceived discrimination; the separate results are reported elsewhere¹⁹.

Validity and reliability

For each ICSEY scale it has been shown that it measures the same psychological construct in all ethnic groups, as all Tucker's phi's, a measure of agreement²⁰, were 0.90 or higher¹⁵. The measures have shown good to excellent internal reliability as well (Cronbach's alphas > 0.70)¹⁵. Cronbach's alphas in our sample were good to excellent for Mastery (0.70), Ethnic Identity (0.81), Perceived discrimination (0.81), Self-esteem (0.83), and Perceived Social Support (0.85). Factor analyses of the cultural distance subscales showed that these could be combined into one factor (loadings 0.49-0.79, eigenvalue 1.9, explained variance 47%). In two sub-samples we investigated inter-rater reliability (N = 23) and test-retest reliability after one week (N = 24) of the scales. Intra-class coefficients were 0.85-0.99 and 0.63-0.96 respectively.

Key informants

For all participants, key informants were asked to complete a short version of the structured interview for their relatives, which included items (4) and (5) of the perceived discrimination scale.

Statistical analyses

Stata version 9.2 was used for all statistical analyses. The matched case-control design required conditional (fixed-effects) logistic regression techniques. First, the total scale score, as well the exploratory and the dichotomous measures, were entered separately in the regression models. Comparisons were made between cases and general hospital controls (100 pairs), and between cases and sibling controls (63 pairs). If there were significant differences between groups, the other variables were added to the regression model to adjust for confounding.

Second, in the total sample, we calculated bivariate Pearson's correlations between total perceived discrimination and the other scale scores. Associations between perceived discrimination and dichotomous variables were tested with χ^2 tests.

Additional analyses addressed the issue of information bias. The scores of participants on items (4) and (5) were compared to the scores provided by their key informants with use of conditional logistic regression. We only used dichotomized scores, because many key informants answered (3) "I don't know". Responses of "Somewhat agree" or "Strongly agree" on any of the items were classified as "Yes", all other scores as "No".

Table 6.1 Sociodemographic characteristics of study sample, by case-control status^a.

	Cases (n=100)	General hospital controls (n=100)	Sibling controls (n=63)
Age, mean (SD)	26.6 (6.7)	27.2 (7.2)	26.5 (8.5)
Male sex	74 (74)	72 (72)	29 (46) ^b
Ethnicity			
Moroccan	29 (29)	30 (30)	20 (32)
Turkish	19 (19)	20 (20)	12 (19)
Surinamese	32 (32)	34 (34)	21 (33)
Other non-Western	20 (20)	17 (17)	10 (16)
Second generation	36 (36)	35 (35)	28 (44)
Single marital status	72 (72)	46 (46) ^b	37 (59) ^b
Level of education			
No / Primary	9 (9)	11 (11)	6 (10)
Secondary	77 (77)	63 (63)	37 (59)
Higher	13 (13)	26 (26)	21 (33)
Unemployed	17 (17)	9 (9)	3 (5) ^c

^a Differences between groups tested with Wald tests in conditional logistic regression analysis.

^b $p < 0.005$, compared to cases.

^c $p < 0.05$, compared to cases.

Results

Of the 146 patients who were eligible for the study, two patients had deceased before the present study was conducted. Twenty-six patients could not be interviewed, because they had remigrated to their home country ($N = 5$), they were too ill during the entire study period ($N = 8$) or because there was no current address available ($N = 13$). Of the 118 patients who were contacted, 18 refused to participate. Thus, 100 patients were interviewed. Of the 168 subjects in the general hospital control group who were matched to the schizophrenia patients, four subjects were physically too ill to be interviewed, one was mentally handicapped, three were excluded because they had a psychotic disorder, and 60 refused to participate. For 15 patients there was no sibling available, because all siblings were too young or lived abroad, patients had no sibling, or patients did not know their current address. Nine patients refused permission to contact their siblings, two patients only had a sibling who had psychotic symptoms. For 11 of the remaining 74 patients, the siblings refused to participate. Thus, siblings of 63 patients could be interviewed. Sociodemographic characteristics of the study sample are shown in Table 6.1.

Fifty two percent of the cases and 42 % of both control groups reported experiences of discrimination (Tables 6.2 and 6.3), but this difference was not statistically significant. The other measures of perceived discrimination did not yield statistically significant dif-

Table 6.2 Odds Ratios of schizophrenia for perceived discrimination, comparisons between cases and matched general hospital controls ^a.

Perceived discrimination	Cases (n=100)	General hospital controls (n=100)	Unadjusted		Adjusted ^b	
			OR	95% CI	OR	95% CI
Dichotomous measure, n (%)	52 (52)	42 (42)	1.50	0.85-2.64	0.92	0.33-2.55
Total scale score, mean (SD)	9.84 (5.70)	8.57 (4.07)	1.05	0.99-1.12	0.96	0.85-1.08
Against own ethnic group, mean (SD)	2.37 (1.66)	2.40 (1.42)	0.98	0.82-1.18	0.74	0.51-1.07
Personal experiences, mean (SD)	7.47 (4.65)	6.18 (3.13)	1.08	1.01-1.17	0.99	0.86-1.13

^a Conditional logistic regression analysis.

^b Adjusted for marital status, unemployment, level of education, cultural distance, ethnic identity, social support, self-esteem, mastery, and cannabis use.

ferences between cases and controls either, except that cases reported more personal experiences of discrimination than general hospital controls (OR per unit increase of the scale = 1.08 [95% CI, 1.01-1.17], Table 6.2).

After adjustment for unemployment, level of education, marital status, cultural distance, mastery, ethnic identity, self-esteem, social support, and cannabis use, there were no statistically significant differences in perceived discrimination between cases and controls (results not shown for comparisons between cases and siblings).

In the total sample, perceived discrimination was reported more often by males than by females (50% versus 37%, $\chi^2=3.98$, $df=1$, $p=0.046$), and by those with a history of cannabis use (55% versus 41% in non-users, $\chi^2=4.69$, $df=1$, $p=0.03$). There were no significant differences in prevalence of discrimination with regard to generation, unemployment, level of education, and marital status. Table 6.4 shows correlations between perceived discrimination and ethnic density, ethnic identity, cultural distance, social support, mastery, and self-esteem. Perceived discrimination was positively correlated with cultural distance, and negatively correlated with ethnic identity, mastery and self-esteem.

Information from key informants was available for 43 cases, 37 siblings and 45 general hospital controls. As was found with the self-report measure, cases were reported to have perceived discrimination somewhat more often than controls (Table 6.5). In all groups,

Table 6.3 Odds Ratios of schizophrenia for perceived discrimination, comparisons between cases and their siblings.

Perceived discrimination	Cases (n=63)	Sibling controls (n=63)	OR	95% CI
Dichotomous measure, n (%)	31 (49)	27 (42)	1.40	0.62-3.15
Total scale score, mean (SD)	9.40 (5.55)	9.21 (5.16)	1.01	0.93-1.09
Against own ethnic group, mean (SD)	2.32 (1.71)	2.49 (1.52)	0.91	0.71-1.18
Personal experiences, mean (SD)	7.08 (4.45)	6.71 (4.09)	1.03	0.93-1.13

Table 6.4 Correlations between perceived discrimination and social contextual factors in the total study sample.

	1.	2.	3.	4.	5.	6.	7.
1. Discrimination	1						
2. Ethnic density	-.11	1					
3. Ethnic identity	-.12 ^a	.18 ^b	1				
4. Cultural distance	.22 ^b	.09	.27 ^b	1			
5. Social support	-.08	.19 ^b	.22 ^b	.00	1		
6. Mastery	-.13 ^a	.12	.18 ^b	-.12 ^a	.25 ^b	1	
7. Self-esteem	-.18 ^b	.07	.25 ^b	.03	.27 ^b	.39 ^b	1

^a $p < 0.05$ ^b $p < 0.01$

the proportions of self-reported perceived discrimination were higher than those reported by their key informants, but these differences were not statistically significant.

Discussion

Racial discrimination has been suggested to explain the consistent finding of an increased incidence of schizophrenia in ethnic minority groups in western Europe⁴, but to date, the association between discrimination and schizophrenia has hardly been studied¹¹. In this case-control study of first-episode schizophrenia among non-Western immigrants, individuals who developed schizophrenia reported somewhat higher rates of perceived discrimination in the year prior to illness onset than their siblings and matched general hospital controls, but the differences were not statistically significant. A considerable proportion of all groups (52 percent of the cases and 42 percent of both control groups) had perceived discrimination.

These results suggest that there may be no direct and strong relationship between perceived discrimination at the individual level and the development of schizophrenia. A previous study showed that the incidence of psychotic disorders in The Hague was higher when ethnic minority groups experienced more discrimination¹¹, and other studies reported associations between perceived discrimination and the prevalence or

Table 6.5 Perceived discrimination^a measured by self-report and key informants.

	Self-report, n (%)	Key-informant, n (%)
Cases (n=43)	9 (21)	7 (16)
Siblings (n=37)	6 (16)	4 (11)
General hospital controls (n=45)	6 (14)	5 (11)

^a Dichotomous measure, assesses personal experiences of teasing, insulting, threats or attacks because of one's ethnic background.

the onset of psychosis⁸⁻¹⁰. The heterogeneity of these findings may depend upon the aspect of discrimination that is studied and the way it is measured⁵, but also upon social and psychological factors that have been shown to influence the perception and impact of discrimination^{6,7,21}.

Measure of discrimination

Racial discrimination adversely affects mental health in at least three different ways⁷. Interpersonal experiences of racist insults or violence have been related to psychological distress, depression, low self-esteem⁵, and, as noted earlier, psychosis^{8,9}. Structural discrimination by institutions, as in employment policies or access to education or housing facilities, also has a deleterious influence on health^{7,22}, not only because it leads to lower socioeconomic status, which has been linked to the increased incidence of schizophrenia among ethnic minorities²³, but also because the gap between aspirations and achievements may give rise to feelings of humiliation and social defeat, factors that may be involved in the etiology of schizophrenia^{24,25}. Finally, awareness of prevailing negative cultural stereotypes has been associated with poor mental health and academic underachievement, independent of personal experiences of racist insults or violence^{21,26,27}. Our measure of discrimination assessed the individual's perceptions of discrimination with five statements that may not have captured all aspects of racial discrimination. Particularly, experiences of institutional racism and negative stereotyping may have been missed. The previous finding of a relationship between the incidence of psychotic disorders and ethnic groups' experiences of discrimination¹¹ suggests that these aspects of discrimination may be relevant for schizophrenia.

Cases may have underreported experiences of discrimination. Recall bias may have occurred because of cognitive impairments due to the illness, or because the recent experience of first psychosis was so overwhelming that memories of negative experiences before onset of illness have faded. This is unlikely to account for the results, however, as the reports of key informants showed a similar pattern to the self-report data (it should be noted that this information was available only for 43 cases) (Table 6.5). Also, a study from the United Kingdom found that, although ethnic minority schizophrenia patients experienced similar numbers of life events to white British patients, they attributed these more often to discrimination²⁸. Thus, there is no evidence that ethnic minority patients would underreport racial discrimination.

Context of discrimination

Given the relatively high prevalence of perceived discrimination in these data, another explanation for the results may be that the experience of discrimination itself is not sufficient, but that the development of schizophrenia depends upon other fac-

tors, such as the social context in which discrimination takes place. Recent studies have shown that the incidence of schizophrenia among ethnic minorities is lower when they live in neighbourhoods with a high percentage of members of their own ethnic group^{13,29}, or where ethnic fragmentation is low³⁰. A mechanism possibly underlying these findings is that pathogenic effects of discrimination are buffered or prevented in high ethnic density neighbourhoods, by social support³¹, social capital³⁰ and strong ethnic identity³², factors that may be greater in high ethnic density neighbourhoods³³. Thus, while the degree of perceived discrimination may be similar among cases and controls, social support and ethnic identity may eventually determine the risk of schizophrenia. If such resources are scarce, the social stress resulting from these difficulties may exceed the coping ability of individuals with a genetic vulnerability to schizophrenia, who often have impaired executive function³⁴. When subjected to such a severe challenge, they may be more likely to develop the disorder³⁵.

This hypothesis is consistent with the directions of the correlations that we found in our data. Perceived discrimination was negatively correlated with ethnic density, ethnic identity, mastery and self-esteem, and positively with cultural distance; ethnic density was positively correlated with ethnic identity and social support; and ethnic identity was positively correlated with social support, cultural distance, mastery, and self-esteem (Table 6.4).

Cannabis use increases the risk of schizophrenia³⁶, and was also correlated with perceived discrimination. It is conceivable that perceived discrimination leads to cannabis use, for instance because individuals may use it to alleviate the stress that is brought about by experiences of discrimination.

Other methodological considerations

The power of study was too low to detect small effects. It was designed to investigate potential explanations for the substantially increased incidence rates of schizophrenia among ethnic minorities (for instance, the incidence rate ratio for first- and second-generation Moroccans in The Hague was 4.0 [95% CI, 2.5-6.3] and 5.8 [2.9-11.4] respectively, compared to the indigenous Dutch population²). To explain an increase of this magnitude requires a causal factor with a strong effect. Thus, even if perceived discrimination at the individual level would be associated with schizophrenia, it is unlikely that it is a strong risk factor in itself.

All consecutive first-episode schizophrenia cases between 2000 and 2005 were eligible for the study, but not all patients participated. It is conceivable that those individuals

who believed to be discriminated against more often refused to participate. However, the same selection bias would occur in the control groups.

The general hospital controls may not have been representative for the general immigrant population, but the choice for a control group selected from immigrants who made contact with non-psychiatric secondary health care services minimized selection bias as a result of pathways to care, as the schizophrenia cases were also recruited from secondary psychiatric services. In addition, the very diverse complaints for which the controls made contact makes it very unlikely that their somatic illness would be related to perceived discrimination.

Conclusion

Perceived discrimination at the individual level was not a strong risk factor for schizophrenia in these data. The relationship between racial discrimination and psychosis may vary with the aspect of discrimination that is studied, and may also depend upon the social context in which discrimination takes place.

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7

Ethnic identity and the risk for schizophrenia in ethnic minorities: a case-control study

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In preparation

Abstract

Background: Previous studies have reported a high incidence of schizophrenia for immigrant ethnic groups in Western Europe. The explanation of these findings is unknown, but is likely to involve social stress inherent to the migrant condition. We investigated whether weak or negative identification with the own ethnic group is a risk factor for schizophrenia in non-Western immigrants.

Methods: Case-control study of first-episode schizophrenia. Cases included all non-Western immigrants who made first contact with a physician for a psychotic disorder in The Hague, the Netherlands, between October 2000 and July 2005, and received a diagnosis of a schizophrenia spectrum disorder (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) (N=100). Two matched control groups were recruited, one among immigrants who made contact with non-psychiatric secondary health care services (N=100), and one among siblings of the cases (N=63). Cognitive and affective ethnic identity in the year before illness onset were assessed with structured interviews. Four identity types were distinguished: integrated, separated, assimilated and marginalized identity. Conditional logistic regression analyses were used to predict schizophrenia as a function of ethnic identity.

Results: Cases had a weak cognitive ethnic identity more often than general hospital controls, (adjusted Odds Ratio [OR] = 4.18, 95% Confidence Interval [CI], 1.89-9.21), and evaluated their ethnic identity as more negative (adjusted OR = 5.07, 95% CI, 2.22-11.57). They more often had an assimilated or a marginalized identity (OR = 4.82 [1.86-12.49] and OR = 2.23 [1.03-4.84] respectively), and less often had a separated identity (OR = 0.17 [0.06-0.48]). Comparisons between cases and siblings largely confirmed these findings.

Conclusions: Weak and negative identification with the own ethnic group may be a risk factor for schizophrenia in immigrants living in a context of social adversity.

Introduction

Schizophrenia is a complex disorder with genetic and non-genetic causes¹, which remain largely unknown. The striking finding of a very high incidence of schizophrenia and other psychotic disorders among ethnic minority groups in western Europe^{2,3} may offer clues to the etiology of schizophrenia. A recent meta-analysis and review of 18 incidence studies of schizophrenia and other psychotic disorders estimated relative risks of 2.7 (95% Confidence Interval, 2.3-3.2) and 4.5 (1.5-13.1) for first- and second-generation immigrants respectively, compared with native populations, and suggested that adverse social experiences of ethnic minority groups may contribute to their elevated risk⁴. Few studies evaluated this hypothesis, and reported that ethnic minority groups' experiences of discrimination were associated with the incidence of schizophrenia in ethnic minority groups⁵, as was living in a neighbourhood with a low proportion of members of one's own ethnic group^{6,7} or with high ethnic fragmentation⁸.

The present study aimed to investigate how such social experiences would result in individuals developing schizophrenia. We focused on ethnic identity, because positive identification with one's own ethnic group may buffer the negative consequences of racial discrimination^{9,10}, is likely to be threatened among members of ethnic minority groups who live isolated from their own ethnic group^{11,12}, and is a strong predictor of mental health and well-being in first- and second-generation immigrants^{13,14}.

A second dimension of group identity is the identity as a member of the larger society (hereafter national or Dutch identity), which is independent of ethnic identity¹⁵; that is, ethnic identity and national identity can both be either positive and strong, or negative and weak¹⁶. An individual who retains a strong ethnic identity while also identifying with the larger society is considered to have an integrated identity. One who has a strong ethnic identity but a weak national identity has a separated identity, whereas one who gives up an ethnic identity and only has a strong national identity, has an assimilated identity. The individual who identifies neither with the own ethnic group nor with the larger society has a marginalized identity¹³.

Integration has been associated with good mental health^{13,17}, and marginalization has been shown consistently to predict low self-esteem and poor mental health^{13,14,18}. Research of the health consequences of separation and assimilation had contradictory results¹⁹, perhaps because the consequences of having these cultural identities depend more upon the social context and upon the aspect of mental health that is studied. There are no studies of the relationship between ethnic identity and schizophrenia, but given the previous findings of a higher risk for second-generation immigrants^{3,4}, who are generally more assimilated than immigrants of the first generation¹⁵, and the findings of a higher risk for immigrants living in low ethnic density neighbourhoods⁶, assimilation may increase the risk of schizophrenia, whereas separation may be protective. This case-

control study of first-episode schizophrenia among non-Western ethnic minorities in The Hague, the Netherlands, was designed to investigate these factors as determinants of schizophrenia. We hypothesized that first- and second-generation ethnic minorities who developed schizophrenia would identify themselves less often and less positive with their own ethnic group, would more often have an assimilated or marginalized identity, and less often a separated or integrated identity.

Methods

Classification of ethnicity

We used the classification of ethnicity as defined by the Netherlands' Bureau of Statistics. If a citizen, or (one of) his or her parents, was born abroad, he or she is assigned to the group of people born in the same country. If the parents were born in different foreign countries, the country of birth of the mother determines the assignment to a particular group.

Participants

Cases

All first- or second-generation immigrants from non-Western countries (of which 85% from Surinam, Morocco, Turkey, or Netherlands-Antilles), aged 18-54 years, who made first contact with a physician in The Hague for a psychotic disorder and received a diagnosis of a schizophrenia spectrum disorder (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) between October 1, 2000 and July 1, 2005, were eligible for the study (N=150). Case-finding procedures and diagnostic protocol of the study have been described elsewhere³. If the patient had been adopted as a child, he or she was excluded (N = 4).

Controls

For each patient, two control subjects were recruited, matched for five-year age-group, sex, and ethnicity (including generation). They were screened for psychotic symptoms (see Measures), and were excluded if these were present (N = 5).

The first control group was recruited among the general ethnic minority population of The Hague. To minimize selection bias as a result of pathways to care, the controls were selected from immigrants who made contact with non-psychiatric secondary health care services. Controls were recruited from the outpatient departments of Internal Medicine and Surgery of a general hospital. The reasons for making contact with these departments differed widely, and included: lipoma or naevus (N = 15), fracture (N = 8),

contusion (N = 11), haemorrhoids (N = 8), sinus pilonidalis (N = 5), anal fissure (N = 5), inflammatory bowel disease (N = 5), diabetes mellitus (N = 5), and other, less frequent diagnoses (N = 38).

The second control group consisted of siblings of the patients, in order to (partially) control for genetic factors.

All participants gave written informed consent for the study. The study was approved by the regional ethics committee. Structured interviews were conducted by a resident in psychiatry (WV) and four trained research assistants. If participants did not speak Dutch sufficiently (N = 9), three trained research assistants, who were native speakers in Turkish, Kurdish, Urdu, Arabic or Berber, conducted the interviews. Because we expected this in advance to concern only a small minority of the sample, we neither developed nor maintained a protocol for translation and back-translation of the questionnaires. Participants were instructed to answer according to their situation in the year before illness onset, the date of which was determined first.

Measures

The relationship between ethnicity and schizophrenia is complex²⁰. Associations between ethnic identity, national identity and schizophrenia may be confounded and mediated by a host of factors. We considered single marital status and low socioeconomic status as potential confounding factors, as these factors have been associated with schizophrenia^{21,22}. Cannabis use, perceived social support, self-esteem and mastery were considered as potential mediating factors, as it is conceivable that these factors are consequences of weak and negative ethnic identity, and may play a role in the pathway to development of schizophrenia²³⁻²⁷.

Most measures were adapted from the International Comparative Study of Ethnocultural Youth (ICSEY), a study among more than 10,000 adolescents from 30 ethnic groups in 13 countries, which included Surinamese, Turkish and Antillean immigrants in the Netherlands¹⁷.

Ethnic and national identity

Various studies on ethnic identity have shown that different aspects of identification can be distinguished, including a cognitive aspect, which involves self-categorization as group member (identification *as*), and an affective aspect, which concerns the emotional evaluation of group membership (identification *with*)²⁸⁻³⁰. We measured cognitive ethnic identity with two statements on self-categorization of ethnicity: "I think of myself as Dutch" and "I think of myself as *ethnic*". Response options ranged from "not at all" (1) to "very much" (5). Scores of three and higher were classified as "Strong", one and two

as “Weak”. Affective identity was measured with the ordinal ICSEY scale of Ethnic and National Identity. This is a 10-item version of the Multi-group Ethnic Identity Measure^{31,32}, with response options ranging from “strongly disagree” (1) to “strongly agree” (5), assessing ethnic and national affirmation, sense of belonging, and feelings about being group member. An example is: “Being part of *ethnic* culture is embarrassing to me”. We calculated the median scores of the Ethnic and National Identity scale, and used these as cut-off points to classify participants as having a positive or a negative affective identity.

Also, participants were assigned to different identity categories. Participants who scored above the median of both ethnic identity and national identity were classified as having an integrated identity. Those with a score above the median of ethnic identity but below the median of national identity had a separated identity; those with a score below the median of ethnic identity but above the median of national identity had an assimilated identity, and those who had a score below the median of both measures had a marginalized identity.

Psychotic symptoms

In control subjects, the psychosis section of the Composite International Diagnostic Interview (CIDI), version 2.1³³, was administered.

Potential confounding factors

Information was noted on marital status (single or else). Socioeconomic status was assessed with level of education (no or primary, secondary, or higher education), employment status (unemployed or else), and parental social class: father’s level of occupation (according to the classification of the Netherlands’ Bureau of Statistics) and father’s level of education (no or primary, secondary, or higher education).

Potential mediating factors

We used the 15-item Rosenberg Self-Esteem Scale (example: “On the whole, I am satisfied with myself”)³⁴, the 6-item ICSEY Mastery Scale, indicating locus of control (example: “When I make plans, I feel certain that I can make them work”)¹⁷, and the 12-item Shortened Social Support Scale (example: “How often does someone shows interest in you?”)³⁵ for perceived social support. Also, lifetime use of cannabis was noted. Use was defined as more than five times.

Key informants

For all participants, key informants were asked to complete a short version of the structured interview for their relatives, which included sociodemographic information, life events, language use, racial discrimination and social behavior.

Validity and reliability of measures

For each ICSEY scale, it has been shown that it measures the same psychological construct in all ethnic groups, as all Tucker's phi's, a measure of agreement³⁶, were 0.90 or higher¹⁷. The measures have shown good to excellent internal reliability as well (Cronbach's alphas > 0.70). Cronbach's alphas in our sample were good to excellent for Mastery (0.70), Ethnic Identity (0.81), National Identity (0.82), Self-esteem (0.83), and Perceived Social Support (0.85). In two sub-samples we investigated inter-rater reliability (N = 23) and test-retest reliability after one week (N = 24) of the scales, with intra-class coefficients of 0.85-0.99 and 0.63-0.96 respectively.

Statistical analysis

Stata version 9.2, was used for all statistical analyses. The matched case-control design required conditional (fixed-effects) logistic regression techniques. The regression models were fitted stepwise. First, each variable was entered separately in the model. Those variables that differed significantly between cases and control groups (with p-values < 0.10) were selected for further analyses. Next, the variables of ethnic identity and national identity, and the four identity types were included with all potential confounding variables. For the variables of ethnic identity and national identity, in a third step, all potential mediating variables were added to the model. Comparisons were made between cases and general hospital controls (100 pairs), and between cases and sibling controls (63 pairs).

Additional analyses addressed the issue of information bias. Scale scores of participants were compared to the scores provided by their key informants with use of conditional logistic regression.

Results

Of the 146 patients who were eligible for the study, two patients had deceased before the present study was conducted. Twenty-six patients could not be interviewed, because they had remigrated to their home country (N = 5), they were too ill during the entire study period (N = 8) or because there was no current address available (N = 13). Of the 118 patients who were contacted, 18 refused to participate. Thus, 100 patients were interviewed. Of the 168 subjects in the general hospital control group who were matched to the schizophrenia patients, four subjects were physically too ill to be interviewed, one was mentally handicapped, three were excluded because they had a psychotic disorder, and 60 refused to participate. For 15 patients there was no sibling available, because all siblings were too young or lived abroad, patients had no sibling, or patients did not know their current address. Nine patients refused permission to contact their siblings,

Table 7.1 Characteristics of study sample, by matched case-control status ^a.

	Cases (n=100)	General hospital controls (n=100)	Cases (n=63)	Sibling controls (n=63)
Age	26.6 (6.7)	27.2 (7.2)	25.9 (6.8)	26.5 (8.5)
Male sex, n (%)	74 (74)	72 (72)	50 (79)	29 (46) ^b
Ethnicity, n (%)				
Moroccan	29 (29)	30 (30)	20 (32)	20 (32)
Turkish	19 (19)	20 (20)	12 (19)	12 (19)
Surinamese	32 (32)	34 (34)	21 (33)	21 (33)
Other non-Western	20 (20)	17 (17)	10 (16)	10 (16)
Second generation, n (%)	36 (36)	35 (35)	27 (43)	28 (44)
Single marital status, n (%)	72 (72)	46 (46) ^b	52 (83)	37 (59) ^b
Level of education, n (%)				
No / Primary	9 (9)	11 (11)	3 (5)	6 (10)
Secondary	77 (76)	63 (63)	48 (76)	37 (59)
Higher	13 (13)	26 (26)	11 (17)	20 (32)
Occupational level father, n (%) ^d				
Low	59 (63)	46 (58)	39 (64)	39 (65)
Middle	26 (28)	28 (35)	17 (28)	15 (25)
High	8 (9)	6 (8)	5 (8)	6 (10)
Level of education father, n (%) ^e				
No / Primary	41 (57)	49 (62)	21 (47)	30 (56)
Secondary	25 (35)	22 (28)	19 (43)	18 (33)
Higher	6 (8)	8 (10)	4 (9)	6 (11)
Unemployed, n (%)	17 (17)	9 (9)	13 (21)	3 (5) ^c
Cannabis use, n (%)	59 (59)	21 (21) ^b	20 (32)	13 (21) ^b
Self-esteem	53.68 (12.12)	60.28 (9.97) ^b	53.65 (12.26)	61.52 (10.13) ^b
Mastery	23.73 (5.21)	24.76 (4.30)	24.73 (4.56)	25.87 (3.66)
Perceived social support	27.95 (8.12)	33.80 (5.86) ^b	28.71 (8.30)	31.10 (6.81)

^a Means (SD), unless otherwise specified.

^b $p < 0.005$, Wald test, conditional logistic regression analysis.

^c $p < 0.05$, Wald test, conditional logistic regression analysis.

^d Information missing for 31 (11.7%) participants.

^e Information missing for 59 (22.3%) participants.

two patients only had a sibling who had psychotic symptoms. For 11 of the remaining 74 patients, the siblings refused to participate. Thus, siblings of 63 patients could be interviewed. Matching for sex and age was often not possible.

Table 7.2 Measures of identity, by matched case-control status^a.

	Cases (n=100)	General hospital controls (n=100)	p	Cases (n=63)	Sibling controls (n=63)	p
Ethnic minority identity, n (%)						
Weak cognitive identity ^b	50 (50)	30 (30)	0.003	29 (46)	20 (32)	0.08
Negative affective identity ^c	64 (64)	35 (35)	0.000	38 (60)	18 (29)	0.001
Dutch identity, n (%)						
Weak cognitive identity ^b	52 (52)	42 (42)	0.08	31 (49)	36 (57)	0.40
Negative affective identity ^c	47 (47)	53 (53)	0.37	30 (48)	48 (76)	0.002

^a Differences between groups tested with Wald tests in conditional logistic regression analysis.

^b Responses “Not at all”, “A little”, or “Somewhat” to the statements: “I think of myself as *ethnic*”, and “I think of myself as Dutch” respectively.

^c Median used as cut-off on scale scores of affective ethnic and Dutch identity.

Characteristics of the study sample are shown in Table 7.1. Compared with controls, cases more often had single marital status, were more often unemployed and had a lower level of education.

Also, cases had lower self-esteem than general hospital controls and siblings in the year before illness onset, and more often had a lifetime history of cannabis use.

In the comparison between cases and general hospital controls, cases more often had a weak cognitive ethnic identity (50% and 30% respectively, $p = 0.003$, Table 7.2). Negative affective ethnic identity was significantly more prevalent in cases, whereas a similar proportion of the groups had a negative affective Dutch identity (Table 7.2). After adjustment for potential confounding factors, weak cognitive ethnic identity was a risk factor for schizophrenia (OR = 4.18, 95% CI, 1.89-9.21), as was negative affective ethnic identity (OR = 5.07, 95% CI, 2.22-11.57) (Table 7.3). After further adjustment for potential mediating factors (Table 7.4), these differences remained statistically significant. The analyses

Table 7.3 Odds Ratios of schizophrenia for weak and negative identity; conditional logistic regression.

	Cases versus general hospital controls ^a			Cases versus sibling controls ^b		
	OR	95% CI	p	OR	95% CI	p
Ethnic identity						
Weak cognitive identity ^c	4.18	1.89-9.21	0.000	1.66	0.53-5.19	0.39
Negative affective identity ^d	5.07	2.22-11.57	0.000	5.27	1.45-19.18	0.01
Dutch identity						
Weak cognitive identity ^c	1.59	0.73-3.44	0.24	0.17	0.03-0.89	0.03
Negative affective identity ^d	0.63	0.32-1.25	0.19	0.14	0.03-0.68	0.01

^a 100 pairs, associations adjusted for marital status, level of education, and unemployment.

^b 63 pairs, associations adjusted for sex, marital status, level of education, and unemployment.

^c Responses “Not at all”, “A little”, or “Somewhat” to the statements: “I think of myself as *ethnic*”, and “I think of myself as Dutch” respectively.

^d Median used as cut-off on scale scores of affective ethnic and Dutch identity.

Table 7.4 Effect of potential mediating factors in the relationship between schizophrenia and identity.^a

	Cases versus general hospital controls			Cases versus sibling controls		
	OR	95% CI	p	OR	95% CI	p
Ethnic minority identity						
Weak cognitive identity	4.18	1.89-9.21	0.000	1.66	0.53-5.19	0.39
additional adjustment for						
Self-esteem	3.53	1.56-8.01	0.003	1.18	0.30-4.56	0.81
Social support	5.01	1.92-13.09	0.001	1.60	0.50-5.11	0.43
Cannabis use	6.08	2.11-17.54	0.001	2.31	0.45-11.91	0.32
All of the above	5.67	1.69-18.99	0.005	2.11	0.33-13.54	0.43
Negative affective identity	5.07	2.22-11.57	0.000	5.27	1.45-19.18	0.01
additional adjustment for						
Self-esteem	4.29	1.84-9.97	0.001	2.63	0.60-11.55	0.20
Social support	3.71	1.57-8.76	0.003	7.13	1.60-31.84	0.01
Cannabis use	3.84	1.64-8.99	0.002	9.14	1.12-74.32	0.04
All of the above	2.53	1.00-6.38	0.05	9.63	0.81-114.38	0.07
Dutch identity						
Weak cognitive identity	1.59	0.73-3.44	0.24	0.17	0.03-0.89	0.03
additional adjustment for						
Self-esteem	1.41	0.61-3.25	0.43	0.07	0.01-0.67	0.02
Social support	1.02	0.42-2.47	0.97	0.11	0.02-0.71	0.02
Cannabis use	1.76	0.67-4.60	0.25	0.09	0.01-0.94	0.04
All of the above	1.09	0.37-3.20	0.88	0.03	0.00-0.79	0.04
Negative affective identity	0.63	0.32-1.25	0.19	0.14	0.03-0.68	0.01
additional adjustment for						
Self-esteem	0.49	0.22-1.06	0.07	0.11	0.02-0.68	0.02
Social support	0.39	0.17-0.90	0.03	0.12	0.02-0.60	0.01
Cannabis use	0.45	0.19-1.06	0.07	0.08	0.01-0.50	0.01
All of the above	0.27	0.09-0.79	0.02	0.02	0.00-0.60	0.03

^a Conditional logistic regression, all associations adjusted for (sex), marital status, level of education, and unemployment; differences tested for statistical significance with Wald tests.

of the identity types showed that cases significantly more often had an assimilated or a marginalized identity, and less often had a separated identity (Table 7.5).

In the comparison between cases and siblings, negative affective ethnic identity predicted schizophrenia (adjusted OR = 5.27, 95% CI, 1.45-19.18), whereas weak cognitive Dutch identity and negative affective Dutch identity were associated with a lower risk of schizophrenia (adjusted OR = 0.17, 95% CI, 0.03-0.89 and OR = 0.14, 95% CI, 0.03-0.68 respectively, Table 7.3). After further adjustment for potential mediating factors, these

Table 7.5 Odds Ratios of schizophrenia for identity types; conditional logistic regression.

Identity type ^a	Cases versus general hospital controls ^b			Cases versus sibling controls ^c		
	OR	95% CI	p	OR	95% CI	p
Integrated	0.53	0.25-1.10	0.09	4.76	0.81-27.91	0.08
Separated	0.17	0.06-0.48	0.001	0.08	0.02-0.41	0.002
Assimilated	4.82	1.86-12.49	0.001	5.42	0.74-39.61	0.10
Marginalized	2.23	1.03-4.84	0.04	3.12	0.37-1.55	0.08

^a Median used as cut-off on scale scores of affective ethnic and Dutch identity. Integrated identity indicates high ethnic and high Dutch identity, separated is high ethnic and low Dutch identity, assimilated is low ethnic and high Dutch identity, marginalized is low ethnic and low Dutch identity.

^b 100 pairs, associations adjusted for marital status, level of education, and unemployment.

^c 63 pairs, associations adjusted for sex, marital status, level of education, and unemployment.

differences increased (Table 7.4). Finally, cases had significantly less often a separated identity than their siblings (Table 7.5).

Information from key informants was available for 43 cases, 38 siblings and 44 general hospital controls. There were no statistically significant differences between the information from the cases and from their key informants. In the sibling and in the general hospital control groups, participants rated their social integration somewhat higher than their key informants did (results not shown, available on request).

Discussion

The increased risk of schizophrenia for ethnic minority groups in Western Europe is a consistent and strong finding ⁴. Adverse social experiences may contribute to this increase ²⁰, but the mechanism by which such experiences would result in individuals developing schizophrenia has yet to be determined. In this case-control study of first-episode schizophrenia among non-Western ethnic minorities, weak and negative identification with the own ethnic group was associated with schizophrenia. Individuals who developed schizophrenia identified themselves less often and less positive with their own ethnic group than general hospital controls in the year before illness onset. They had a more positive affective Dutch identity than the matched controls, more often an assimilated or a marginalized identity, and less often a separated identity.

Comparisons between cases and their siblings largely confirmed these findings, particularly with regard to negative affective ethnic identity and separated identity. In addition, weak and negative Dutch identity was associated with lower risk of schizophrenia. Although this case-sibling design only partially controls for genetic factors, the similarity of the results in the two control groups makes it very unlikely that genetic vulnerability for schizophrenia can account for the findings.

Methodological issues

Several limitations are inherent to the case-control design. First, since the interviews were conducted (shortly) after the first episode of schizophrenia, the results may have been influenced by the illness. The prodromal stage or early symptoms of schizophrenia may have led to weak and negative ethnic identity, and to preference for assimilation. We have tried to minimize this potential bias by instructing the patients that the interview concerned the period before the onset of illness, the date of which was determined with participants first. Although this instruction does not rule out reverse causality entirely, we do not believe that it is a likely explanation for the results. It is difficult to understand why the illness would lead to lower self-categorization as ethnic, and not to lower identification as Dutch; to negative feelings about being ethnic, and to more positive feelings about being Dutch; to assimilation, and not to separation.

The issue of reverse causality also applies to the potential mediating factors. Based on the literature, we postulated a priori that perceived social support, mastery, self-esteem and cannabis use may be mediators in the relationship between ethnic identity and schizophrenia, but we acknowledge that the direction of some of the associations may also be reversed. For instance, low social support from family and other members of the own ethnic group may lead to a weak and negative ethnic identity.

Second, it is difficult to assess experiences, behaviors and opinions accurately in retrospect. This applies to all participants, because we interviewed the controls on the same time period as the case they were matched to, but problems with recall are likely to be larger for cases than for controls, as a result of cognitive impairments caused by the illness. Additional analyses showed that there were no significant differences between scores of cases and their key informants (available on request), suggesting that recall bias cannot explain the results entirely.

The comparisons between cases and siblings may have been underpowered, because only 63 siblings participated, and the matched case-control design required conditional analyses. This had large consequences for the statistical power, as the pairwise analysis implied that the data of 37 cases could not be used in these comparisons.

All consecutive first-episode schizophrenia cases between 2000 and 2005 were eligible for the study, but not all patients participated. It is conceivable that those individuals who were oriented more towards their own ethnic group lost contact with psychiatric services in the early phase of treatment, or that they refused to participate. However, the same selection bias would occur in the control groups.

The general hospital controls may not have been representative for the general immigrant population, but the choice for a control group selected from immigrants who

made contact with non-psychiatric secondary health care services minimized selection bias as a result of pathways to care, as the schizophrenia cases were also recruited from secondary psychiatric services. In addition, the very diverse complaints for which the controls made contact makes it very unlikely that their somatic illness would be related to ethnic identity.

We had also included the ICSEY measures of acculturation strategies in the study¹⁷, measuring preference for assimilation, integration, separation and marginalization in five domains of life: cultural traditions, language, marriage, social activities, and friends. The scales, however, had low Cronbach's alphas in our study sample (0.34-0.58), indicating that these measures were not very reliable. Therefore we did not report the results in the main analyses, although the results support the other findings, as cases had significantly higher scores on assimilation and marginalization than both control groups (results available on request).

Interpretation

The limitations notwithstanding, our results suggest that a weak and negative ethnic identity is associated with the onset of schizophrenia in ethnic minorities. Belonging to an ethnic minority group subjected to discrimination and negative stereotyping has previously been associated with the incidence of schizophrenia⁵, and represents a threat to self-esteem and social identity¹². Individuals may respond to this threat by asserting identification with their group, and by seeking positive distinctiveness from the majority group, which enhances self-esteem³⁷, prevents or buffers stress^{9,15}, and has been associated with psychological well-being^{13,14,16,38}. An opposite response to this threat is trying to downplay ethnic identity, striving to leave the low status minority group and to join the dominant group¹². The boundaries between ethnic groups are difficult to cross, however, which means that this strategy often increases rather than resolves the threat¹⁵. It is likely to be associated with feelings of powerlessness and humiliation³⁹, and with experiences of an undeserved gap between aspirations and achievements⁴⁰. The social stress resulting from this threat is a severe cognitive and emotional challenge, which may exceed the coping ability of individuals with a genetic vulnerability to schizophrenia, who often have impaired executive function⁴¹. When subjected to such a severe challenge, they may be more likely to develop the disorder^{39,42}.

The effect of ethnic identity was partly mediated by cannabis use and perceived social support. Cannabis use has been related to the onset of schizophrenia²⁴ and may be a behavioral consequence of the social stress of negative ethnic identity. Indeed, in our total sample, cannabis use was correlated to negative affective ethnic identity ($r = .22$, $p < 0.005$).

Lack of ethnic identification may also lead to social isolation and less social support (correlation between negative affective ethnic identity and social support: $r = -.22$, $p < 0.005$). Social support increases access to normalizing explanations for anomalous perceptual experiences and abnormal beliefs, that are present in individuals at high risk for developing psychosis²⁵. Whereas social isolation may contribute to the acceptance of a psychotic appraisal of these early abnormal mental states, a social network may have a normalizing function, thus preventing transition into psychosis⁴³.

Biological plausibility

The neural diathesis of schizophrenia may entail special vulnerability to develop psychosis in the context of social stress, through a dysfunctional dopamine system⁴⁴. Dopamine is likely to play a central role in the pathophysiology of schizophrenia⁴⁵. Repeated experiences of social stress may sensitize the mesolimbic dopamine system^{46,47}, which means that there may be a dopamine hyperresponsivity to stress in individuals who are genetically at risk for schizophrenia⁴⁸.

Previous findings

These results are consistent with reports of a higher incidence of schizophrenia among ethnic minorities living in neighbourhoods where their own ethnic group comprises a small proportion of the population⁶⁻⁸. Those who live in low ethnic density neighbourhoods must contend with the triple burden of increased exposure to prejudice, reduced social support, and fewer possibilities for positive ethnic identification¹¹, factors that are likely to increase the social stress of minority status.

Previous studies have found variable and modest associations of low family socioeconomic status and incidence of schizophrenia^{22,49}, and have suggested that socioeconomic disadvantage may contribute to the increased incidence among immigrants⁵⁰. In our data, there were no significant differences in parental socioeconomic status between the groups, but it was very low in all groups. Low socioeconomic status may represent a situation of social exclusion²², particularly for individuals who compare themselves predominantly with the advantaged majority group^{12,15}.

Finally, a study in the United Kingdom among ethnic minorities found that prolonged separation from (one of the) parents during childhood was a risk factor for schizophrenia⁵¹. Although parental separation may be an indicator of several early adverse social experiences, it is not unlikely that ethnic identity formation and racial socialization is more often compromised in children growing up within single-parent families⁵².

Conclusions

Weak and negative identification with the own ethnic group may be a risk factor for schizophrenia in ethnic minorities experiencing social adversity, whereas separation

may be protective. The findings also have broader implications in suggesting that social factors can play a role in the etiology of schizophrenia, and that social stress of minority status may explain the increased incidence of schizophrenia in immigrants.

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8

Cannabis use and genetic predisposition for schizophrenia: a case-control study

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Abstract

Background: Cannabis use increases the risk for schizophrenia. Part of this association may be explained by genotype-environment interaction (schizophrenia genes controlling sensitivity to cannabis psychotogenic effects), and part of it by genotype-environment correlation (schizophrenia genes controlling likelihood of cannabis use). While there is some evidence for genotype-environment interaction, the issue of genotype-environment correlation has not been explored. We investigated whether cannabis use is associated with schizophrenia, and whether gene-environment correlation contributes to this association, by examining the prevalence of cannabis use in groups with different levels of genetic predisposition for schizophrenia.

Method: Case-control study of first-episode schizophrenia. Cases included all non-Western immigrants who made first contact with a physician for a psychotic disorder in The Hague, the Netherlands, between October 2000 and July 2005, and received a diagnosis of a schizophrenia spectrum disorder (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) (N=100; highest genetic predisposition). Two matched control groups were recruited, one among siblings of the cases (N=63; intermediate genetic predisposition), and one among immigrants who made contact with non-psychiatric secondary health care services (N=100; lowest genetic predisposition). Conditional logistic regression analyses were used to predict schizophrenia as a function of cannabis use, and cannabis use as a function of genetic predisposition for schizophrenia.

Results: Cases had used cannabis significantly more often than their siblings and general hospital controls (59%, 21% and 21% respectively). Cannabis use predicted schizophrenia (adjusted OR cases compared to general hospital controls = 6.2 [2.4-15.8], adjusted OR cases compared to siblings = 17.3 [1.7-176.9]), but genetic predisposition for schizophrenia did not predict cannabis use (adjusted OR intermediate predisposition compared to lowest predisposition = 1.1 [95% CI, 0.4-3.4]).

Conclusions: Cannabis use was associated with schizophrenia, but there was no evidence for genotype-environment correlation.

Introduction

Several studies have reported that exposure to cannabis during adolescence and young adulthood increases the risk for schizophrenia later in life ¹. A recent meta-analysis calculated that the pooled odds ratio of the association between cannabis use and psychosis of all published prospective studies was 2.1 (95% CI, 1.7-2.5) ². This is a moderate association, but there is evidence of underlying heterogeneity of the relative risk associated with other vulnerability factors ^{3,4}. In particular, there may be an interplay between genetic liability for psychosis and cannabis use with regard to the development of psychosis ². There are two main types of gene-environment interplay. First, genetic differences between people may change sensitivity to environmental influences (*genotype-environment interaction*, or GxE) ⁵. Recent studies reported that a functional polymorphism in the catechol-O-methyltransferase (COMT) gene moderated the effect of cannabis use on the risk for psychosis ^{6,7}, suggesting that GxE may play a role. Second, genetic differences may affect the environments people choose or experience (*genotype-environment correlation*, or rGE) ⁵. Genetic predisposition for psychosis thus may directly affect cannabis use. Some studies reported that psychosis liability predicts future cannabis use, but effect sizes were small and not consistently statistically significant ^{4,8}. In addition, because in these studies liability for psychosis was defined as high scores on paranoid ideation and psychoticism at baseline, the association with cannabis use may indicate not only rGE, but also self-medication for distress or early symptoms of psychosis.

We conducted a case-control study of first-episode schizophrenia in The Hague, the Netherlands, and included three groups with a different genetic predisposition for psychosis: first-episode schizophrenia patients (highest predisposition), their siblings (intermediate predisposition), and matched general hospital controls (lowest predisposition). We excluded control subjects who had ever had any psychotic symptom, and assessed life-time cannabis use among participants. Two questions were addressed: (1.) is cannabis use associated with development of schizophrenia, that is, do cases use cannabis more often than both control groups before illness onset, and (2.) is there evidence for rGE, independent of phenotypic expression of predisposition for psychosis, that is, do siblings use cannabis more often than general hospital controls?

Methods

Participants

Cases

This paper uses data from a study among ethnic minorities in The Hague. All first- or second-generation immigrants from non-Western countries (of which 85% from Surinam, Morocco, Turkey, or Netherlands Antilles), aged 18-54 years, who made first contact with a physician in The Hague for a psychotic disorder and received a diagnosis of a schizophrenia spectrum disorder (DSM IV: schizophrenia, schizophreniform disorder, schizoaffective disorder) between October 1, 2000 and July 1, 2005, were eligible for the study. Case-finding procedures and diagnostic protocol of the study have been described elsewhere ⁹. If the patients had been adopted as a child, they were excluded (N = 4).

Controls

For each patient, two control subjects were recruited, matched for five-year age-group, sex, and ethnicity (including for first- or second-generation immigrant status). They were screened for psychotic symptoms (see Measures), and were excluded if these were present (N = 5). The first control group consisted of siblings of the patients. If a patient had more than one sibling, the same-sex sibling closest in age was selected. The second control group was recruited among the general ethnic minority population of The Hague. To minimize selection bias as a result of pathways to care, the controls were selected from immigrants who made contact with non-psychiatric secondary health care services. Controls were recruited from the outpatient departments of Internal Medicine and Surgery of a general hospital.

All participants gave written informed consent for the study. The study was approved by the local ethics committee.

Measures

In control subjects, the psychosis section of the Composite International Diagnostic Interview (CIDI), version 2.1 ¹⁰, was administered. Lifetime use of cannabis and other substances was assessed with the section on drugs of the Comprehensive Assessment of Symptoms and History (CASH) ¹¹. Participants were instructed to answer about their pattern of use before illness onset, the date of which was determined first. Individuals with lifetime use of five times or more were considered as exposed. We combined psychostimulants, opiates, cocaine, and psychedelic drugs into a group of "other drugs". Information was noted on marital status (single or else). Socioeconomic status was

assessed using level of education (no or primary, secondary, or higher education) and employment status (unemployed or else).

Statistical analysis

Stata version 9.2, was used for all statistical analyses. In order to answer the first research question, we calculated Odds Ratios (OR) and 95% Confidence Intervals (95% CI) for schizophrenia, with cannabis use as independent variable. Conditional (fixed-effects) logistic regression techniques were required in order to take the matched case-control design into account. Comparisons were made between cases and general hospital controls (100 pairs), and between cases and sibling controls (63 pairs). Second, in order to investigate genotype-environment correlation, siblings were compared to general hospital controls, with unconditional logistic regression analysis, including cannabis use as dependent variable and genetic predisposition for schizophrenia as predictor of cannabis use. All associations were adjusted (through matching or as covariate in the model) for age, sex, marital status, level of education, unemployment, and other drug use.

Results

Of the 146 patients who were eligible for the study, two patients died before the study was commenced. Twenty-six patients could not be interviewed, because they had re-migrated to their home country (N = 5), they were too ill during the entire study period (N = 8) or because there was no current address available (N = 13). Of the 118 patients who were contacted, 18 refused to participate. Thus, 100 patients were interviewed. Of the 168 subjects in the general hospital control group who were matched to the schizophrenia patients, four subjects were physically too ill to be interviewed, one was mentally handicapped, three were excluded because they had a psychotic disorder, and 60 refused to participate. For 15 patients there was no sibling available, because all siblings were too young or lived abroad, patients had no sibling, or patients did not know their current address. Nine patients refused permission to contact their siblings, two patients only had a sibling who had psychotic symptoms. For 14 of the remaining 74 patients, the sibling who was matched to the case refused to participate; in three of these cases, another sibling agreed to participate. Thus, for 63 cases, a sibling could be interviewed. Characteristics of the study sample are shown in Table 8.1.

Fifty-nine percent of the cases, 21% of their siblings and 21% of the general hospital controls had used cannabis (Table 8.2). Conditional logistic regression analyses showed that the differences between cases and the other groups were statistically significant.

Table 8.1 Characteristics of study sample, by matched case-control status ^a.

	Cases (n=100)	General hospital controls (n=100)	Sibling controls (n=63)
Age, mean (SD)	26.6 (6.7)	27.2 (7.2)	26.5 (8.5)
Male sex, n (%)	74 (74)	72 (71)	29 (46) ^d
Ethnicity			
Moroccan	29 (29)	30 (30)	20 (32)
Turkish	19 (19)	20 (20)	12 (19)
Surinamese	32 (32)	34 (34)	21 (33)
Other non-Western	20 (20)	17 (17)	10 (16)
Second generation, n (%)	36 (36)	35 (35)	28 (44)
Single marital status, n (%)	72 (72)	46 (46) ^d	37 (59) ^d
Level of education, n (%)			
No / Primary	9 (9)	11 (11)	6 (10)
Secondary	77 (77)	63 (63)	37 (59)
Higher	13 (13)	26 (26)	21 (33)
Unemployed, n (%)	17 (17)	9 (9)	3 (5) ^c
Other drug use, n (%) ^b	20 (20)	4 (4) ^d	5 (8) ^c

^a Differences between cases and other groups tested by Wald test, conditional logistic regression analysis.

^b Lifetime use (more than five times) of psychostimulants, opiates, cocaine, or psychedelic drugs.

^c $p < 0.05$, compared to cases.

^d $p < 0.005$.

After adjustment for confounders, cannabis use remained a statistically significant predictor of schizophrenia in the comparison between cases and general hospital controls.

There was no difference between siblings and matched general hospital controls in prevalence of cannabis use (Table 8.2). Genetic predisposition for schizophrenia did not predict cannabis use, as the OR of cannabis use for siblings versus general hospital controls was 0.8 (95% CI, 0.4-1.9) before and 1.1 (95% CI, 0.4-3.4) after adjustment (Table 8.3).

Table 8.2 Odds Ratios of schizophrenia, by cannabis use ^a.

	Cannabis use ^b	Unadjusted	Adjusted ^c
	n (%)	OR (95% CI)	OR (95% CI)
Cases (n=100)	59 (59)	6.4 (2.9-14.3)	6.2 (2.4-15.8)
General hospital controls (n=100)	21 (21)	1.0	1.0
Cases (n=63)	43 (68)	30.0 (4.1-220.0)	17.3 (1.7-176.9)
Sibling controls (n=63)	13 (21)	1.0	1.0

^a Using conditional logistic regression.

^b Lifetime use, defined as more than five times.

^c Adjusted for other drug use, (sex), marital status, level of education and unemployment.

Table 8.3 Odds Ratios of cannabis use^a, by genetic predisposition for schizophrenia^b.

	Unadjusted	Adjusted ^c
	OR (95% CI)	OR (95% CI)
Highest predisposition (n=100)	7.6 (3.4-17.0)	9.7 (3.0-31.0)
Intermediate predisposition (n=63)	0.8 (0.4-1.9)	1.1 (0.4-3.4)
Lowest predisposition (n=100)	1.0	1.0

^a Lifetime use, defined as more than five times.

^b Using (un-)conditional logistic regression.

^c Adjusted for other drug use, sex, marital status, level of education, and unemployment.

Discussion

Cannabis use was associated with schizophrenia in this case-control study of first-episode schizophrenia. Cases had used cannabis approximately three times more often than their siblings and matched general hospital controls. Sibling controls had not used cannabis more often than general hospital controls, in spite of their higher genetic predisposition for schizophrenia.

Our results add to the evidence that cannabis use is associated with an increased risk of schizophrenia¹. The magnitude of the effect was substantially larger than that was calculated in the meta-analysis of results from prospective studies². Although patients had been instructed to report on cannabis use *before* illness onset, it is possible that they did not recognize early prodromal symptoms as such, creating the possibility that in some patients the period of cannabis assessment may have overlapped with the onset of schizophrenia. The association between cannabis and psychosis may be bi-directional, that is, cannabis may not only be a causal factor in the pathway to schizophrenia, but may be used as self-medication for distress or early prodromal symptoms, as has been suggested by previous findings⁸.

It is very unlikely that the association between cannabis and schizophrenia can be explained by genotype-environment correlation. Unlike other studies^{3,4}, we used unaffected siblings and unrelated controls who had never had any psychotic symptom to classify degree of genetic predisposition for schizophrenia, rather than measures of psychoticism or delusional ideation. This allowed us to investigate genotype-environment correlation independent of a possible self-medication effect. The comparison between siblings and unrelated controls showed that higher genetic predisposition for schizophrenia did not lead to a higher rate of lifetime cannabis use.

Table 8.4 Lifetime use of cannabis^a, per ethnic group, stratified for case-control status.

Ethnic group ^b	Cannabis use, n (%)				Cases versus controls, OR (95% CI) ^c
	Total	Cases	Sibling controls	General hospital controls	
Surinam (n=87)	34 (45)	21 (66)	4 (19)	9 (26)	8.0 (2.3-27.7)
Turkey (n=52)	11 (21)	8 (42)	2 (17)	1 (5)	10.4 (1.3-85.2)
Morocco (n=79)	34 (43)	20 (69)	5 (25)	9 (30)	9.8 (2.2-43.1)
Other non-Western countries (n=47)	14 (30)	10 (50)	2 (20)	2 (12)	10.6 (1.3-85.1)

^a Use defined as more than five times.

^b First and second generation combined.

^c Cases versus combined control groups, conditional logistic regression, unadjusted.

Methodological issues

The inclusion of this study was limited to first- and second-generation non-Western immigrants, which raises the question whether the findings can be generalized across (other) ethnic groups. It is conceivable that the correlation between genetic factors and cannabis use is different in majority and minority populations, or that some ethnic groups may be more vulnerable to the psychotogenic effects of cannabis than other groups. We did not have data on the Dutch majority population, but when we stratified for ethnicity in our data, the associations between cannabis and (predisposition for) schizophrenia were very similar in the Surinamese, Turkish and Moroccan groups (Table 8.4). Turkish participants had used cannabis less often than Moroccan, Surinamese and other non-Western participants. The OR of cannabis use for Turkish participants compared to other ethnic groups was 0.44 (95% CI, 0.21-0.90).

Difficulties in the recruitment of siblings may have caused selection bias, as the siblings who refused to participate may have used cannabis more often than those who agreed to be interviewed. However, although the difference between cases and siblings in the prevalence of cannabis use was large, there was not even a suggestion of a difference between the two control groups, making it unlikely that selection bias could have had a major impact on the results. Even if one assumes that all refusing sibs had been cannabis users, the difference in cannabis use between siblings and controls would not have been statistically significant (rates would have been 35% and 21% respectively, unadjusted OR, 1.84 [95% CI, 0.87-3.90]). Rather, the large difference between cases and siblings in the rate of cannabis use is compatible with an underlying mechanism of gene-environment interaction, suggesting that genetic predisposition alone may not be sufficient to cause psychotic disorder.

Drug use was assessed with information provided by participants themselves. This may have led to underreporting, although in the Netherlands the attitude towards substance

use is quite open. In addition, the researchers were not involved with patients' treatment, and did not provide any information to the physician responsible without the patients' consent.

Participants were asked whether they had ever used drugs before illness onset. There may have been recall bias as a result of this retrospective assessment, particularly in the group of cases, because impaired cognitive functioning is one of the features of schizophrenia¹². If anything, however, this is likely to have led to underestimation of the prevalence of cannabis use in cases.

The general hospital controls may not have been representative for the general immigrant population, but the choice for a control group selected from immigrants who made contact with non-psychiatric secondary health care services minimized selection bias as a result of pathways to care, as the schizophrenia cases were also recruited from secondary psychiatric services. Moreover, the very diverse complaints for which the controls made contact (ranging from fractures to anal fissures) makes it unlikely that their somatic illness would be related to cannabis use.

Conclusion

Our findings support the hypothesis that cannabis use is a risk factor for schizophrenia, and suggest that genetic predisposition for schizophrenia does not increase the risk of cannabis use. Associations between cannabis use, genetic predisposition for psychosis, and schizophrenia cannot be attributed to genotype-environment correlation, but are most likely due to interactions between genetic factors and cannabis.

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9

General discussion

Main findings

The first-contact incidence study of psychotic disorders in The Hague (Chapter 2) showed that first- and second-generation immigrants have an increased risk for schizophrenic disorders, compared to native Dutch (age- and gender-adjusted IRR, 2.3; 95% CI, 1.7-3.0 and 2.5; 95% CI, 1.7-3.7 respectively). When ethnic groups were investigated separately, the risk was significantly increased for immigrants from Morocco, Surinam, and Other non-Western countries, but not for immigrants from Turkey. The risk was particularly high for Moroccan males (first generation IRR 4.0; 95% CI, 2.5-6.3, second generation IRR, 5.8; 95% CI, 2.9-11.4). Second-generation immigrants from non-Western countries had a higher risk than those of the first generation (IRR, 1.5; 95% CI, 1.0-2.3).

When the results from three more years (2002-2005) were added, the seven year risk for psychotic disorders among Turkish immigrants was significantly increased as well (IRR, 1.8; 95% CI, 1.3-2.5). The incidence among Moroccan and Surinamese immigrants remained high.

Immigrants from Morocco not only had the highest risk of schizophrenia, they were also most severely ill (Chapter 3). Those who made first treatment contact for a psychotic disorder in The Hague had significantly higher total psychopathology and negative symptom scores than native Dutch patients, and more often presented with persecutory delusions, bizarre behavior and visual hallucinations. Also, Moroccan and Turkish patients more often met the criteria for a current depressive episode. Other ethnic minority groups had levels of psychopathology similar to those of native Dutch.

The differences in incidence among ethnic groups depended upon the social context in which people live. Two aspects of the social context were associated with the incidence of psychotic disorders. First, the neighborhood context strongly influenced the risk of psychotic disorders among immigrants (Chapter 4). Compared to native Dutch, the incidence among immigrants increased when the proportion of members of their own ethnic group in the neighborhood diminished (adjusted IRR, 0.95, $\chi^2 = 15.04$, $df = 1$, $p = 0.0001$). In low ethnic density neighborhoods, immigrants had a markedly increased incidence (adjusted IRR, 2.36; 95% CI, 1.89-2.95), whereas in high ethnic density neighborhoods, the incidence rate was not significantly higher than that of native Dutch (IRR, 1.25; 95% CI, 0.66-2.37). Similar patterns were evident for Moroccan, Surinamese, and Turkish immigrant groups examined separately. In each group, the incidence rate of psychotic disorders was significantly increased only among immigrants living in low ethnic density neighborhoods. The Moroccan group exhibited the highest incidence rates of psychotic disorders, and the difference between low and high ethnic density neighborhoods was largest for Moroccan immigrants.

Second, the incidence varied among ethnic minority groups according to degree of perceived discrimination: the incidence was higher when groups perceived more discrimination (Chapter 5). Compared with native Dutch, the age- and sex-adjusted IRRs of psychotic disorders for degrees of perceived discrimination (high, medium, low and very low respectively) among ethnic minority groups were 4.00 (95% CI 3.00-5.35), 1.99 (1.58-2.51), 1.58 (1.10-2.27) and 1.20 (0.79-1.84).

At the individual level, a matched case-control study of first-episode schizophrenia in non-Western ethnic minority groups investigated whether schizophrenia was associated with aspects of acculturation. Individuals who developed schizophrenia reported somewhat higher rates of perceived discrimination in the year prior to illness onset than their siblings and matched general hospital patient controls, but the differences were not statistically significant (Chapter 6). A considerable proportion of all groups (52 percent of the cases and 42 percent of both control groups) had perceived discrimination. Perceived discrimination was positively correlated with cultural distance and cannabis use, and negatively with ethnic identity, self-esteem and internal locus of control.

Weak and negative identification with one's own ethnic group was associated with schizophrenia (Chapter 7). Individuals who developed schizophrenia identified themselves less often and less positively in the year before illness onset with their own ethnic group than general hospital controls. They had more often an assimilated or a marginalized identity than the matched controls, and less often a separated identity. Comparisons between cases and their siblings largely confirmed these findings, particularly with regard to negative affective ethnic identity and separated identity.

Finally, cannabis use was strongly associated with schizophrenia (Chapter 8). Cases had used cannabis approximately three times more often (59%) than their siblings (21%) and matched general hospital controls (21%). Sibling controls had not used cannabis more often than general hospital controls, in spite of their higher genetic predisposition for schizophrenia. Turkish participants had used cannabis less often than those from the other ethnic minority groups, but the association between cannabis and schizophrenia did not vary substantially with ethnicity.

These results suggest that the increased incidence of schizophrenia and other psychotic disorders among first- and second-generation immigrants can be understood by taking into account the social and cultural context in which immigrants live. This increased incidence is likely to be determined by factors on multiple levels, including the neighborhood, the ethnic group, and the individual. Specifically, living in a context of low ethnic density, belonging to a group that experiences a high degree of discrimination, and having a weak and negative identification with one's own ethnic group increased the risk of psychotic disorders.

Methodological considerations

Before discussing the meaning of the findings, it is necessary to consider the main methodological issues of the studies presented in this thesis.

Selection bias

In the incidence study, we sought to identify and diagnose every citizen of The Hague aged 15-54 years who made first contact with a physician for a possible psychotic disorder. Although there was extensive collaboration with the local general practitioners, psychiatrists and residents in psychiatry to gain access to every possible case, the question remains whether treated incidence rates represent the “true” incidence. It is often argued that, given the severity of the disorder, most schizophrenia cases will make contact with health care services, but virtually all studies of the incidence of schizophrenia are based on treated cases, which makes it difficult to estimate the proportion of psychotic cases that do not come to the attention of professionals¹. Thus, to the extent that cases of psychotic disorders remain untreated, underestimation of true incidence is inevitable.

For the interpretation of the results presented in this thesis, it is important to consider whether there may have been differences in the degree of case ascertainment among ethnic groups. The processes by which patients enter into the health care system differ by ethnic group^{2,3}. For instance, black individuals in the United Kingdom come into contact with psychiatric services more frequently through a criminal justice agency or through emergency services than do white individuals and are more often admitted compulsorily^{2,4}. In the Netherlands, Mulder and colleagues found an association between non-Western ethnicity and compulsory admission⁵, which was related to a greater severity of psychiatric symptoms in ethnic minorities than in Dutch natives, more danger to others as perceived by clinicians, less motivation for treatment and lower level of social functioning⁵. The differences may indicate ethnic bias by Dutch clinicians, but may also be caused by delay in help seeking by immigrants, due to different beliefs about mental illness or due to impaired social networks, which have been shown to influence entry into treatment⁶. In spite of the differences in pathway to care among ethnic groups, however, there is no evidence that the duration of untreated psychosis is longer among immigrants than among native populations, neither in the United Kingdom⁷ nor in The Hague⁸.

If there was any ascertainment bias in our study, it is likely to be in the direction of a lower rather than a higher treated incidence rate among immigrants. This is a problem in the interpretation of the ethnic density findings, because, if immigrants clustered in high density neighborhoods are less likely than those living in low ethnic density

neighborhoods to use Dutch health services when they develop psychotic symptoms, this could produce an artifactual ethnic density effect. Additional analyses of our data suggested that this is unlikely (see Chapter 4).

In the case-control study, selection bias may have occurred in the recruitment of the controls. We did not use a random sample of the general immigrant population, but recruited immigrant patients from the outpatient surgery and internal medicine departments of a general hospital in the city center. The advantage of this approach is that the controls and the cases had in common the fact that they made contact with secondary health care. On the other hand, the controls may not have been representative of the general immigrant population. For instance, they may have more often a weak ethnic identity and a higher degree of perceived discrimination, because these factors have been associated with several physical problems^{9,10}. The great diversity of complaints for which the controls made contact, however, including hemorrhoids, lipomas and contusions, makes it unlikely that their somatic illnesses were related to ethnic identity, discrimination or acculturation. If there were a relationship, it would lead to underestimation of the effect of ethnic identity and perceived discrimination.

Confounding

The analyses of the relationship between schizophrenia and ethnicity in the incidence study were adjusted for age and sex, but could not be adjusted for individual socioeconomic status, because this information was not available for the population. As noted earlier, the association between the incidence of schizophrenia and low socioeconomic status is subject to an ongoing debate. Study results were inconsistent and generally inconclusive¹¹⁻¹³, and the question remains whether low socioeconomic status is a cause of schizophrenia, or a consequence of deteriorated social functioning which is a part of the illness, or both^{14,15}. We were able to take neighborhood socioeconomic level into account; adjustment of the incidence rates for this variable had only a minor effect⁸. In addition, the ethnic density findings suggest that low individual socioeconomic status is not a likely explanation for the increased incidence of psychotic disorders among immigrants. It is difficult to see how low ethnic density, which was associated with an increased risk of schizophrenia, would be related consistently to low individual socioeconomic status, because the socioeconomic level of neighborhoods with a high proportion of non-Western immigrants was much lower than that of primarily Dutch, low ethnic density, neighborhoods.

The investigation of the relationship between the incidence of schizophrenia and ethnic minority groups' degree of perceived discrimination is very vulnerable to confounding, because ethnic groups differ in many aspects other than perceived discrimination. It is

possible that other characteristics of the ethnic groups, which are strongly associated with perceived discrimination, are a part of the explanation for the increased incidence rates, rather than discrimination. We have discussed several potential confounding factors in Chapter 5, and return to this issue in the section on the interpretation of the findings (paragraph 9.3). Given the difficulties of controlling for confounding factors at the group level, and the much weaker association we have found between schizophrenia and perceived discrimination at the individual level, it remains inconclusive whether there is a causal relationship between schizophrenia and perceived discrimination.

Confounding in the case-control study concerns the relationship between schizophrenia and individually perceived discrimination (Chapter 6), ethnic identity (Chapter 7) and cannabis use (Chapter 8). We have prevented some confounding by matching controls to the cases by five-year age-group, sex and ethnicity (including generation). In addition, the measures in the case-control study included several potential confounding factors, among which individual socioeconomic status and single marital status. In the studies on perceived discrimination and ethnic identity, we further adjusted for cannabis use, self-esteem and social support. Associations remained statistically significant after adjusting for these factors.

A long period of separation from parents in childhood has been associated with the incidence of schizophrenia, particularly among African-Caribbeans in the United Kingdom¹⁶. Also, high paternal age at birth is a risk factor for schizophrenia in offspring¹⁷. These factors were measured in the case-control study, and did not differ statistically significantly between cases and controls (results not presented).

We have tried to take genetic predisposition for schizophrenia into account by including siblings of the cases as a control group. Since siblings share only half of their genes, it was only partially possible to control for genetic predisposition. However, on average, siblings have a higher genetic predisposition for schizophrenia than unrelated general hospital controls, an assumption we have used to investigate the correlation between genetic predisposition for schizophrenia and cannabis use.

Reverse causality

All results were obtained from cross-sectional studies, which approach limits the possibility to make causal inferences from the data. Some of the associations in this thesis may be explained by reverse causality. The ethnic density findings could have been affected by this issue, as individuals with psychotic disorders may have moved from high to low density neighborhoods prior to their first treatment contact, perhaps driven by prodromal symptoms of their illness, which include social withdrawal¹⁸. However, in The Hague, moving from a high to a low ethnic density neighborhood generally means moving to a neighborhood with a higher socioeconomic level, whereas the prodrome

of schizophrenia is associated with downward social mobility¹². We have discussed this in more detail in Chapter 5.

In the case-control study, by definition, the interviews with schizophrenia patients were conducted after the onset of illness. It is conceivable that the symptoms of schizophrenia lead to weak and negative ethnic identity, perhaps as a result of paranoid ideations towards members of the own ethnic group, or due to an inability to maintain social relationships. Nevertheless, it is difficult to understand why the illness would only lead to lower self-categorization as ethnic, and not to lower identification as Dutch; or to negative feelings about being ethnic, and to more positive feelings about being Dutch; to assimilation, and not to separation.

Cannabis use might also be a consequence of schizophrenia rather than a cause, because it may be used as self-medication for symptoms of psychosis¹⁹. There has been a heavy debate on this issue, but several prospective studies found an association between cannabis use and psychosis, which remained after excluding all individuals at baseline who had ever had a psychosis-like experience²⁰. It is most likely that both the self-medication hypothesis and the causal hypothesis are true²¹.

Generalizability

The findings presented in this thesis should be generalized across countries and other ethnic groups with caution, because the sociohistorical context and political climate of the larger society and of each ethnic group are to some extent unique, and affect the social status, perceptions of discrimination, ethnic density, acculturation orientation and ethnic identity of immigrants²². The results clearly demonstrate that the specific social and cultural context influences the risk of schizophrenia.

With regard to the larger society, Bourhis and colleagues distinguished four types of state integration policies, ranging from a *pluralism* ideology, that promotes multiculturalism and considers it to be of value to the larger society for immigrants to maintain their cultural heritage, to an *ethnist* ideology, which expects immigrants to reject their own ethno-cultural identity for the sake of adopting not only the public, but also the private values and culture of the majority population²³. In the Netherlands, the official policy has been one of pluralism, but recently, attitudes have changed towards a greater insistence on adaptation to the Dutch culture²⁴. This attitude may reflect the *assimilation* ideology, which requires immigrants to abandon their cultural and linguistic distinctiveness and adopt the core public values of the majority population²³. A growing part of the population, however, appears to support the ethnist ideology, as this part only wants to accept immigrants as rightful members of the society when they give up private ethno-cultural values that are considered to be a threat to the larger society. In a more open and pluralist society (such as Canada, that is often referred to as an example of a country with a successful multicultural, pluralist integration policy²²), the relation-

ship between the incidence of schizophrenia among immigrants and the aspects of the social context that we have studied might be different.

With regard to specific ethnic groups, their characteristics are important in the context of acculturation and the risk of schizophrenia, as has been shown in the results of group-level perceived discrimination (Chapter 4). The vitality and social cohesion of immigrant groups influence their position in society, their perceptions of discrimination and exclusion, and their mental health²⁵⁻²⁷. This will be discussed in detail in the following section.

Meaning of findings

The results in this thesis suggest that social factors contribute to the onset of schizophrenia in immigrants, and may explain their increased risk of psychotic disorders. Of the hypothesized factors listed in the Introduction (Table 1.2), we have found that the increased incidence of schizophrenia among ethnic minorities strongly depended upon neighborhood ethnic density and upon the degree to which ethnic groups perceive discrimination. However, we did not find a statistically significant association with perceived

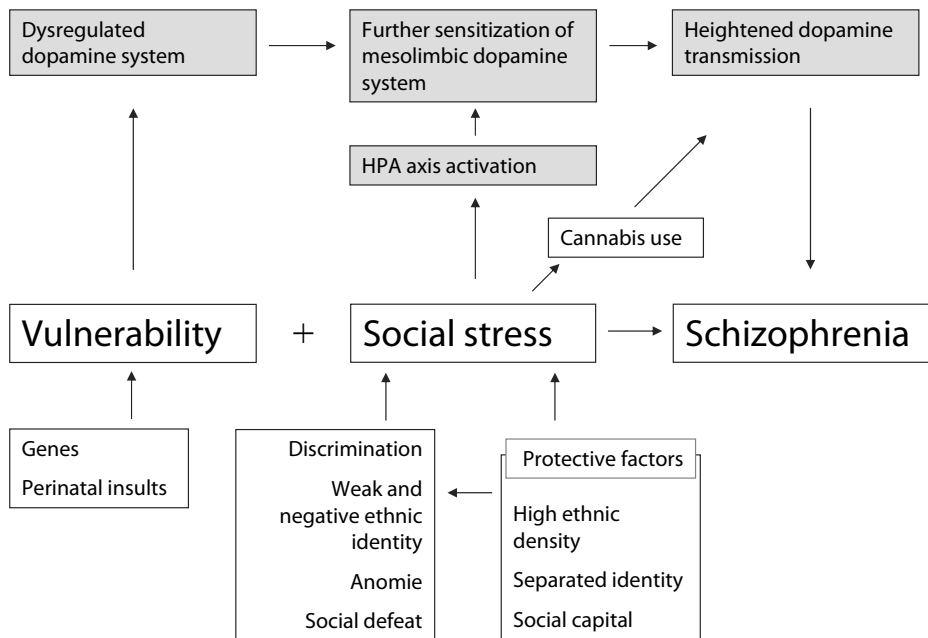


Figure 9.1 Etiological model of schizophrenia in ethnic minorities.

discrimination at the individual level. More research is needed to investigate whether there is a causal relationship between schizophrenia and perceived discrimination.

Low neighborhood socioeconomic level did not explain the high rates of psychotic disorders among immigrants, nor was low socioeconomic status a strong predictor of schizophrenia in individuals. A weak and negative ethnic identity was associated with schizophrenia, whereas maintaining a strong orientation towards one's own ethnic group was protective, as a separated identity was associated with a lower risk of schizophrenia.

We propose that the factors that were found to be relevant may all represent a situation of chronic social stress, which might precipitate schizophrenia in individuals who have a (genetic) predisposition for the illness^{28,29}. The etiological model of schizophrenia in immigrants following from this hypothesis is shown in Figure 9.1. In the next paragraphs, elements of this model are discussed, and placed in a broader perspective.

Adverse social experiences

The high prevalence of persecutory delusions and depression among Moroccan patients (Chapter 3) is consistent with hypotheses that adverse social experiences are part of the explanation of the increased incidence. Cognitive psychological theories state that people with persecutory delusions are preoccupied with the intentions of others, and misinterpret social interactions and events³⁰. When social experiences are negative and threatening, people may be more likely to develop paranoid ideations and depressive feelings³¹, particularly when they feel left out or powerless, or perceive themselves to be in a lower social rank than others^{32,33}. For ethnic minorities and immigrants, experiences of discrimination or a negative ethnic identity may be associated with these characteristics of negative social comparison and threat, which thus may induce paranoid ideation and depression.

The social context

The findings of neighborhood ethnic density (Chapter 4) and group-level perceived discrimination (Chapter 5) suggest that the social context strongly influences the incidence of psychotic disorders among immigrants. A density effect on health has been found among a range of social groups, including ethnic minority groups, religious affiliations, as well as occupational classification³⁴. It has most often been associated with psychiatric admissions, but also with emotional disturbance³⁵, deliberate self harm³⁶ and prevalence of psychiatric symptoms³⁷. Evidence lends credence to a more general hypothesis of "fit", namely that individuals with a particular social characteristic who live in areas where that characteristic is less common have higher rates of psychopathology than those living in areas where that characteristic is common³⁸. In one older study, the

effect was mediated by the experience of prejudice, of being different, from a feeling of an absence of belongingness, and social isolation³⁵.

The association between degree of discrimination perceived by immigrant groups and the incidence of psychotic disorders in these groups (Chapter 5) supports and extends the ethnic density literature. Racial or ethnic discrimination is an important aspect of the everyday social context in which immigrants live^{39,40}, and has a pervasive adverse influence on health^{10,41}, particularly if support from members of one's own ethnic group is low⁴², which is likely to be the case in low ethnic density neighborhoods. Moroccans perceived the most discrimination of all ethnic groups⁴³ and had the highest rate of schizophrenia (Chapter 2 and 5); the difference in incidence between low and high ethnic density neighborhoods was largest for Moroccan immigrants (Chapter 4). Thus, immigrants who live in a low ethnic density environment have an increased risk of schizophrenia, particularly if they belong to an ethnic group experiencing a high degree of discrimination.

Anomie and social capital

Since the nineteenth century, sociological theories have acknowledged that the social context influences individual mental health. Durkheim introduced the concept of *anomie*, defined as a condition of society that is characterized by an absence or diminution of standards or values, caused by lack of social rules and weakening of social regulation⁴⁴. According to Durkheim, anomie is associated with feelings of alienation and purposelessness, and may even lead to suicide⁴⁴. The level of anomie varies by country and over time, but also by social group within a country. It is conceivable that anomie is higher among immigrant groups than among majority populations, because social structures in ethnic minority communities are less complete and more often compromised²⁶. Differences in anomie may also be found among ethnic groups within immigrant populations. In the Netherlands, for instance, there are many more Turkish than Moroccan political or religious organizations⁴⁵, and, in contrast to the Turkish community, the Moroccan ethnic group has been described as guarded and distrustful, not only towards other ethnic groups, but also towards other Moroccans⁴⁶. These characteristics may reflect differences in social regulation within these groups, and parallels the high rate of schizophrenia among Moroccans, and the relatively low rate among Turks (Chapter 2).

Anomie may thus be an alternative explanation for the differences in incidence of schizophrenia among ethnic groups, but it might also influence ethnic minority groups' degree of perceived discrimination, because ethnic support and vitality of ethnic minority communities, which are likely to be low when the degree of anomie is high, may buffer the perceptions of discrimination in ethnic minorities^{42,47}.

Faris and Dunham⁴⁸ already recognized in the thirties the importance of social disorganization in the onset of schizophrenia. More recent reports support this proposition, as associations have been found between rates of psychosis and the number of unmarried persons in a neighborhood^{49,50}, residential mobility⁵¹ and ethnic fragmentation⁵².

Social capital has been proposed as an umbrella concept to describe social relationships within societies or groups of people. In a way, it may be considered as the opposite of anomie, as it has been characterized as “the glue that holds society together”⁵³. Social capital is an inherently ecological, contextual construct, involving community networks, civic engagement, local sense of belonging and mutual trust, solidarity, reciprocity, and norms of cooperation^{54,55}. Low social capital has been associated with increased mortality rates⁵⁶ and higher rates of self-reported psychiatric morbidity⁵⁷. One pilot study across electoral wards in London found an inverse relationship between social cohesion and rates of schizophrenia⁵⁸. A study in Maastricht did not find an association between social capital and the incidence of treated schizophrenia⁵⁹, but recently, Kirkbride and colleagues reported a relationship between the incidence of non-affective psychoses and neighborhood social capital, as measured by voter turnout in local elections⁵², as well as a U-shaped relationship between the incidence of schizophrenia and ethnic density⁵². Using more sophisticated survey data on social cohesion and trust, they found a non-linear association between the disorder and social capital, with the highest incidence of schizophrenia observed in neighborhoods with either “low” or “high” levels of social capital. The researchers concluded that “social capital may be associated with the incidence of disorder, possibly by buffering the risk of psychoses in some areas or increasing the risk for individuals not able to access this form of capital”⁶⁰. Thus, ethnic minorities who live in low ethnic density neighborhoods may have diminished access to social capital, while social stress might be increased for them because they belong to a group experiencing discrimination.

Perceived discrimination

In our case-control data, the prevalence of perceived discrimination at the individual level was high, but perceived discrimination did not predict schizophrenia. We have discussed the possible explanations for this finding extensively in Chapter 6. It is conceivable that our measure of perceived discrimination did not capture all relevant aspects of discrimination, but it is also possible that there is no causal relationship between perceived discrimination and schizophrenia, in spite of our group-level findings (Chapter 5) and the results of a prospective study in the Netherlands, which found an association between perceived discrimination and the onset of delusional ideations⁶¹. Further research is needed to resolve this issue.

Given the relatively high prevalence of perceived discrimination among cases and controls alike, another possibility is that the relationship between schizophrenia and

individually perceived discrimination may depend upon other factors that either result from discrimination, or influence the perception and impact of discrimination^{39,41,62}. These factors may include anomie and social capital at the group level or the neighborhood level (see previous paragraph), and cannabis use and a weak and negative ethnic identity at the individual level. The latter two factors were associated with perceived discrimination (Chapter 6) as well as with schizophrenia (Chapters 7 and 8).

Cannabis use

Cannabis use during adolescence and young adulthood increases the risk for schizophrenia later in life²⁰. The findings on cannabis (Chapter 8) add to the evidence that cannabis is a risk factor for schizophrenia, and suggest that genetic predisposition for schizophrenia does not increase the risk of cannabis use. Associations between cannabis use, genetic predisposition for psychosis and schizophrenia cannot be attributed to genotype-environment correlation, but are most likely due to interactions between genetic factors and cannabis. The similarity among all the ethnic minority groups in the odds ratios for schizophrenia by cannabis use suggests that different sensitivity to cannabis is an unlikely explanation for the heterogeneity in incidence rates of schizophrenia among ethnic groups. Rather, differences in prevalence of cannabis use among ethnic groups may contribute to this heterogeneity, because we have found that Turkish participants in general used cannabis less often than participants from the other ethnic groups, which is consistent with their relatively lower risk of schizophrenia (Chapter 2). Unfortunately, there are no reliable data from population surveys on cannabis use among ethnic minority groups in the Netherlands⁶³. A previous study in The Hague reported that ethnic minorities patients who made first contact for a psychotic disorder did not have higher rates of substance misuse than patients from the native population, and did not find significant differences in the prevalence of cannabis use among ethnic minority patients⁶⁴, but a recent study in the Netherlands found that Moroccan, Surinamese and Antillean male immigrants, but not Turkish immigrants, had a higher risk of first contact for any drug use disorder⁶⁵.

Goal-striving and social defeat

The sociologist Robert Merton expanded on Durkheim's idea of anomie, and focused on the imbalance between the desires and means of individuals⁶⁶. He suggested that anomie is common in a society when there is a significant discrepancy between the cultural goals commonly professed and what is actually achievable in everyday life, and argued that anomie could lead to deviant behavior and mental illness⁶⁷. Ethnic minority groups, having a disadvantaged position and being discriminated against, may experience a particularly large gap between their goals and the opportunities to achieve them, and

thus may be at higher risk for mental illness. This gap may be perceived even more by immigrants living in low ethnic density neighborhoods.

In the 1950's, Kleiner, Parker and Tuckman used this sociological theory to explain social class differences in the rates of schizophrenia. They found that the rates of schizophrenia were higher among individuals above the median education of their respective occupational group than the rates of those below the median ⁶⁸, and observed in a study of black rural south - urban north migration in the USA that the rates of schizophrenia in Pennsylvania were significantly higher for blacks born in the north than for those migrating from the south ⁶⁹. They suggested that this excess might be related to the higher expectations of the former and to their consequent disappointment. Thus, not low social status *per se*, but frustration, caused by a discrepancy between aspirations and achievements, may be associated with schizophrenia ^{68,70}.

This hypothesis has remained largely untested. One small study in the 1970's in the United Kingdom found that West Indian schizophrenia patients had significantly higher levels of goal striving coupled with expectations of assimilation than English patients and healthy West Indian controls ⁷¹, but one case-control study of goal striving and schizophrenia among African Caribbean and Indian immigrants did not support the hypothesis ⁷². Recently, Selten and Cantor-Graae proposed that the long-term experience of *social defeat*, defined as a subordinate position or as 'outsider status' ⁷³, may be an explanation for the increased incidence of schizophrenia among immigrants. Conceptually, this relates closely to the frustration of the gap between aspirations and achievements, as they state that "defeat may be more frequent in immigrants whose notions concerning the ease of upward mobility are thwarted by the opportunities currently available in Western society" ⁷³.

Ethnic identity and acculturation

Frustration and experiences of defeat make it difficult to develop and maintain a coherent and positive social identity ^{34,35,74}.

For Erik Erikson, the founding father of ego identity theory, identity refers to a subjective feeling of sameness and continuity that provides individuals with a stable sense of self and serves as a guide to choices in key areas of one's life ⁷⁵. Identity is not something that individuals automatically have. Rather, an identity develops over time, beginning in childhood, through a process of "reflection and observation" ⁷⁵ that is particularly salient during adolescence and young adulthood but may continue through adulthood and is expected to lead to a resolution or an achieved social identity ⁷⁶.

For first- and second-generation immigrants, ethnic identity is a salient aspect of social identity, not only because their ethnic and cultural background may be important to themselves, but also because they are often defined and judged by others in these terms ⁷⁷. According to the Social Identity Theory (SIT), individuals strive to achieve or to main-

tain a positive social identity, which is based to a large extent on favorable comparisons that can be made between one's own group and other groups⁷⁸. When social identity is unsatisfactory, individuals strive either to leave their existing group and join a more positively distinct group, or to make their existing group more positively distinct⁷⁸. Experiences of discrimination, exclusion and defeat give rise to unfavorable comparisons with the majority group, and thus threaten the positive social identity of immigrants. Individuals may respond to this threat by trying to leave the low status minority group and to join the majority group, but the boundaries between ethnic groups are difficult to cross, which means that this strategy often increases rather than resolves the threat⁷⁹. Another option is strengthening identification with and orientation towards the own ethnic group, in order to seek positive distinctiveness from the majority group (an example is the "black is beautiful" movement among African-Americans in the USA), or to compare oneself with other social groups *within* one's own ethnic group, rather than with the majority group⁷⁹. Several studies showed that a strong, positive ethnic identity is related to psychological well-being among immigrants⁸⁰⁻⁸², may buffer negative consequences of discrimination^{42,83} and enhances self-esteem⁴⁷.

Consistent with the hypotheses presented above, the results of the case-control study suggest that a weak and negative ethnic identity increases the risk of schizophrenia, as does an assimilated or marginalized identity, whereas a strong and predominant orientation towards one's own ethnic group (separated identity) may be protective (Chapter 7). In the face of discrimination and social adversity, it may be essential for first- and second-generation immigrants to retain a positive identification with their own ethnic group and to seek positive distinctiveness from the majority group.

Other research from the Netherlands on mental health of immigrants is generally in line with these findings. Cultural ambivalence, defined as loss of positive bonding with migrant culture while a positive bonding with the host culture has not yet been established, was a risk factor for mental health problems among young Turkish adults, but in this study, ethnic identity (measured by self-categorization as ethnic and/or as Dutch) was not associated with poor mental health⁸⁴. Moroccans accepting both their own and Dutch culture reported a higher level of well-being than those rejecting their own culture and adapting to Dutch culture, but this relationship was not found among Turkish immigrants⁸⁵. Moroccans who adopted integration evaluated their ethnic identity as more positive than those who opted for assimilation⁸⁶. Among young Moroccans, perceived minority vitality, relationships with other Moroccans and a perception of tolerance of the majority predicted lower acculturative stress²⁷, while higher perceived discrimination was associated with lower self-esteem⁸⁷. First-generation Surinamese, Moroccan and Turkish immigrants in Amsterdam, however, reported an association between mental well-being and command of the Dutch language and experience with

Dutch society⁸⁸. On the other hand, cultural traditionalism, as a domain of acculturation, was associated with the absence of mental disorders, whereas the feeling of loss of cultural values predicted the presence of these disorders⁸⁸.

Biological plausibility

There is general consensus that heightened dopaminergic transmission plays a central role in schizophrenia⁸⁹. This hypothesis was originally based on the observations that dopamine receptor antagonists alleviate symptoms of the illness, while dopamine agonists can induce psychotic symptoms⁹⁰. Several studies demonstrated that (untreated) schizophrenia patients have an increased mesolimbic dopamine release after acute amphetamine challenge^{91,92}, suggesting an abnormal responsiveness of dopaminergic neurons. The question remains what causes this hypersensitivity to dopamine. It has been speculated that dopamine dysregulation arises from genetic factors, such as the valine-to-methionine (Val/Met) polymorphism in the Catechol-O-methyl transferase (COMT) gene, which is involved in dopamine metabolism⁹³. Dopamine dysregulation might also be caused by early environmental insults such as prenatal infections, malnutrition or obstetric complications, and by social stress in adolescence or early adult life²⁹. Several neurobiological models suggest links between stress, the hypothalamic-pituitary-adrenal (HPA) axis and dopamine activity^{94,95}. Animal experiments have shown that exposure to stress as well as the biological induction of HPA activation enhance the behavioral response of rats to dopamine agonists^{95,96}, and lead to mesolimbic dopaminergic hyperactivity⁹⁷. Thus, social stress may lead to (further) dysregulation of the dopamine system through an augmenting effect of the HPA axis on dopamine synthesis and release⁹⁵. At the same time it is likely that there is a reciprocal effect such that heightened sensitivity to dopamine influences HPA activation and thus renders the individual hyperresponsive to stress⁹⁵, consistent with recent human studies that found that individuals who are genetically vulnerable to psychosis are more emotionally and behaviorally sensitive to daily life stress than healthy controls^{98,99}.

Consequently, if the results of the animal experiments can be extended to humans, it is possible that chronic exposure social stress leads to disturbances in dopamine function and further to the development of psychosis.

Implications

Research

The work presented in this thesis makes clear that the social context matters in the etiology of schizophrenia. This perspective was present in epidemiological research until the mid-twentieth century, but thereafter, risk factor studies, designed to estimate the effect

of an exposure to a certain factor on the disease risk of individuals predominated¹⁰⁰. In these studies, the broad social context was held constant and was not included within the research framework¹⁰⁰. Only recently has the notion reemerged that differences in schizophrenia rates among groups cannot be explained by studies of risk factors alone^{50,52,101}. Future research should incorporate both individual risk factors and contextual factors. One of the areas for this eco-epidemiological approach^{102,103} would be racial discrimination. We have studied the effects of discrimination at the group level and the individual level, but our results were inconclusive. More research is needed to understand the relationship between perceived discrimination and schizophrenia. It may be worthwhile to investigate the effects of perceived discrimination simultaneously at the individual level and at the group level. A third level of research would be cross-national, in which the influence of state integration policies and attitudes of majority populations could be evaluated. Also, the thus far unproven hypothesis that increased exposure to discrimination may underlie the ethnic density effect should be investigated.

An important issue is the way discrimination is conceptualized and measured. Research on the effects of discrimination on health is only "in its infancy"¹⁰⁴, and most measures have been poorly validated, were only developed for a single ethnic minority group, or did not capture all relevant aspects of discrimination^{39,41}. For instance, the effects of negative stereotypes and stereotype threat on health have not been investigated directly, while these aspects of discrimination are omnipresent and powerful, influence social identity¹⁰⁵ and thus may contribute to the development of psychosis.

Our results suggest that ethnic identity may be an important factor in the onset of schizophrenia among immigrants. This finding warrants further study. First, prospective studies are needed, to disentangle cause and effect, but also because ethnic identity is a dynamic characteristic that develops and changes over time⁷⁶. Ethnic identity should be measured in high risk individuals, to investigate whether transition to psychosis is predicted by weak and negative ethnic identity.

Second, if ethnic identity is a determinant of schizophrenia in immigrants, a more general concept of social identity should be investigated among non-immigrants as well. This could be done by studying identity achievement in first-episode schizophrenia patients, or, preferably, in high risk individuals, perhaps relating this to neuropsychological functioning. Again, multi-level studies, which should include dimensions of social capital⁵², may help to elucidate the complex pathways to schizophrenia. The hypothesis of "fit", namely that individuals with a particular social characteristic who are living in areas where that characteristic is less common, have higher rates of schizophrenia than those living in areas where that characteristic is common³⁸ deserves further testing, as does the social defeat hypothesis⁷³.

We have studied differences across social groups (ethnic groups and neighborhoods) and differences between individuals within groups as determinants of schizophrenia, but other levels should also be studied, as the levels encompass each other, and have intimate links to each other ¹⁰². We have already mentioned the national level, which influences the position and status of ethnic minority groups and thus of individuals within these groups. In the other direction, future studies should incorporate differences among individuals, with regard to genes, the dopamine system, and brain structures. Particularly, gene-environment interactions may play an important role. With the present increasing knowledge of which genes contribute to schizophrenia ¹⁰⁶, this is a promising area of research.

Prevention and treatment

If future research would confirm that having a weak and negative ethnic identity contributes to the onset of schizophrenia among ethnic minorities, preventive strategies could be developed. In the last decade, efforts have been made to identify individuals with a high risk of psychosis ¹⁰⁷, and interventions have been developed to prevent transition to psychosis ¹⁰⁸. Psychological interventions mainly use psycho-educational strategies and cognitive techniques targeted at early positive symptoms ²⁶, but this approach may be too general. Recently, Nelson and colleagues have argued that the subjective experiences of high risk individuals have been neglected, which neglect has limited possibilities for prospective identification and prevention of psychotic disorders ¹⁰⁹. Interventions aimed at exploring social identity issues and developing a secure and positive social identity may provide a more specific target for prevention. In some first- and second-generation immigrants, a strong and positive ethnic identity may prevent psychotic breakdown.

Ethnic identity may be a focus in the treatment of first-episode schizophrenia in immigrants as well. Strengthening of ethnic identity may help immigrants to get a “grip on life”, which has been hypothesized to be related to recovery in schizophrenia ¹¹⁰ (as cited in ²⁶). Stronger ethnic identity may also buffer the negative effects of the stigma of psychiatric illness, which is a severe burden for schizophrenia patients, and perhaps particularly for patients from ethnic minorities ^{111,112}.

Another recommendation for the treatment of immigrant patients concerns depression. The large proportions of Moroccan and Turkish patients in our study meeting the criteria for a current depressive episode suggests substantial co-morbidity of depression in these immigrant groups, a situation to which explicit attention should be paid. Also, in cognitive behavioral therapy, delusions are challenged by investigating the evidence for the beliefs held by patients. Treatment of persecutory delusions in immigrant patients may require addressing the adverse social experiences that have led to negative sche-

matic models of the self and the world, in order to influence the psychological processes that maintain the delusions and prevent the falsification of these delusional ideas.

Finally, if further studies would find more evidence for causal relationships between schizophrenia, ethnic density, anomie and social capital, interventions might be developed to diminish social isolation, to increase social capital and facilitate access to this capital. These interventions may include strategies to strengthen social structures within immigrant groups and within neighborhoods. Local authorities and immigrant organizations might initiate strategies to diminish anomie and to increase social cohesion and mutual trust, although it is a long road to a society with vital ethnic minority communities that are integrated into local social life, with socially cohesive neighborhoods, and with a general belief that ethnic minorities are of value to the society as a whole. In any case, each intervention should be evaluated carefully, in order to measure its effectiveness in the prevention of psychotic disorders.

Conclusions

In conclusion, the findings provide insight into the increased incidence of schizophrenia and other psychotic disorders among immigrants. High incidence rates were found among all non-Western immigrant groups, and were particularly high for first- and second-generation Moroccans (Chapter 2). Findings of a high prevalence of persecutory delusions and depression among Moroccan patients were consistent with the hypothesis that adverse social experiences contribute to this increased incidence (Chapter 3). The social context in which immigrants live strongly influenced their risk of psychotic disorders. The incidence was increased among immigrants living in neighborhoods with a low proportion of members of their own ethnic group (Chapter 4), and was associated with the ethnic groups' degree of perceived discrimination (Chapter 5). At the individual level, perceived discrimination by individuals was not a determinant of schizophrenia (Chapter 6), but a weak and negative ethnic identity strongly predicted schizophrenia (Chapter 7), whereas a separated identity was associated with a lower risk. Cannabis use predicted schizophrenia, but this association was similar in all ethnic groups (Chapter 8). Differences in incidence rates might be related to differences in cannabis use at the population level, as Turkish participants used cannabis less often than other groups, consistent with their relatively low risk of schizophrenia.

Thus, the results presented and discussed in this thesis suggest that social and cultural factors contribute to the increased incidence of schizophrenia and other psychotic disorders among first- and second-generation immigrants. This increased incidence is likely to be determined by factors on multiple levels, including genes, the individual, the

ethnic group, the neighborhood, and the larger society. The factors that were found to be relevant may all represent a situation of chronic social stress, which might precipitate schizophrenia in individuals who have a (genetic) predisposition for the illness. More research is needed to elucidate the complex and interrelated biological, psychological and social pathways to schizophrenia.

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Samenvatting

In veel landen zijn verschillen in gezondheid tussen etnische groepen beschreven. De incidentie van schizofrenie en andere psychotische stoornissen is hoog bij etnische minderheidsgroepen in een aantal landen in West-Europa. In Nederland hebben eerste- en tweede-generatie immigranten uit Marokko, Suriname en de Nederlandse Antillen een verhoogd risico op schizofrenie ten opzichte van de meerderheidsbevolking. Tot op heden is nog geen verklaring voor deze bevindingen gevonden. Een hoge incidentie in de landen van herkomst, selectieve migratie, diagnostische bias, of variatie in het voorkomen van mogelijke risicofactoren zoals obstetrische complicaties of blootstelling aan virussen, verklaren het hogere risico van immigranten niet. In toenemende mate denken onderzoekers dat negatieve sociale ervaringen van immigrantengroepen een verklaring vormen. Sociaal-economische achterstand, langdurige scheiding van de ouders tijdens de jeugd, etnische dichtheid, sociale desorganisatie van de wijk, raciale of etnische discriminatie, acculturatiestrategieën, en een zwakke etnische identiteit zijn geopperd als factoren die zouden kunnen bijdragen aan de verhoogde incidentie, maar slechts enkele studies hebben een paar van deze hypothesen onderzocht.

Dit proefschrift geeft meer inzicht in de verhoogde incidentie van schizofrenie bij eerste- en tweede-generatie immigranten, door de sociale context van schizofrenie bij immigranten te onderzoeken, zowel op individueel niveau als op groepsniveau, en door aspecten van acculturatie als mogelijke determinanten van schizofrenie te bestuderen.

In hoofdstuk 2 beschrijven we incidentiecijfers van schizofrenie in etnische groepen. Een eerste-contact incidentie-onderzoek van psychotische stoornissen in Den Haag liet zien dat het risico op een schizofrenie-spectrum stoornis was verhoogd voor eerste- en tweede-generatie immigranten uit Marokko, Suriname, en Overige niet-Westerse landen. Het risico was in het bijzonder verhoogd voor tweede-generatie immigranten en voor Marokkaanse mannen, en was relatief laag voor Turkse immigranten.

Hoofdstuk 3 rapporteert etnische verschillen in symptomen bij het eerste behandelcontact. Immigranten uit Marokko hadden niet alleen het hoogste risico op schizofrenie, Marokkaanse patiënten hadden ook ernstiger symptomen dan Nederlandse patiënten, en presenteerden zich vaker met achtervolgingswanen, bizar gedrag en visuele hallucinaties. Marokkaanse en Turkse patiënten voldeden vaker aan de criteria voor een depressieve episode.

Hoofdstukken 4 en 5 laten de invloed zien van twee aspecten van de sociale context op de incidentie van psychotische stoornissen.

Ten eerste, de context van de wijk was geassocieerd met het verhoogde risico op psychotische stoornissen bij immigranten (Hoofdstuk 4). Vergeleken met autochtone Nederlan-

ders was de incidentie het meest verhoogd bij immigranten die in wijken woonden waar hun eigen etnische groep een klein deel van de bevolking uitmaakte. In wijken met een lage etnische dichtheid hadden immigranten een duidelijk verhoogd risico, terwijl de incidentie niet significant hoger was dan onder autochtone Nederlanders in wijken met een hoge etnische dichtheid.

Ten tweede, de incidentie varieerde bij etnische groepen met de mate van ervaren discriminatie (Hoofdstuk 5). Met behulp van gegevens uit een bevolkingsonderzoek en aantallen meldingen van discriminatie in Den Haag werden de etnische groepen als volgt ingedeeld naar mate van ervaren discriminatie: hoog (Marokko), medium (Nederlandse Antillen, Suriname, Overige niet-Westerse landen), laag (Turkije), of heel laag (Westerse landen). De incidentie van psychotische stoornissen was hoger in etnische groepen die meer discriminatie rapporteerden, onafhankelijk van sociaal-economische achterstand van de wijk.

Vervolgens wordt de rol van sociale en culturele factoren als potentiële risicofactoren voor schizofrenie beschreven. Een gematchte case-controle studie van de eerste episode van schizofrenie in niet-Westerse etnische minderheidsgroepen onderzocht of aspecten van acculturatie waren geassocieerd met schizofrenie. Individuen die schizofrenie hadden gekregen, rapporteerden een wat hogere mate van ervaren discriminatie in het jaar voorafgaand aan het begin van de ziekte dan hun broers en zussen en gematchte ziekenhuiscontroles, maar deze verschillen waren niet statistisch significant (Hoofdstuk 6).

Een zwakke en negatieve identificatie met iemands eigen etnische groep was een sterke determinant van schizofrenie (hoofdstuk 7). Individuen die schizofrenie hadden gekregen, identificeerden zichzelf minder vaak en minder positief met hun eigen etnische groep in het jaar voorafgaand aan het begin van de ziekte dan de controles. Een gesepareerde identiteit, gedefinieerd als een positieve identificatie met de eigen etnische groep maar niet met de Nederlandse meerderheidsgroep, was geassocieerd met een lager risico op schizofrenie.

Hoofdstuk 8 exploreert associaties tussen cannabis, genetische predispositie voor schizofrenie, en etniciteit. Cases hadden voorafgaand aan de ziekte ongeveer drie keer zo vaak cannabis gebruikt dan hun broers en zussen en gematchte ziekenhuiscontroles. Broers en zussen van schizofreniepatiënten hadden niet vaker cannabis gebruikt dan ziekenhuiscontroles, ondanks hun sterkere genetische predispositie voor schizofrenie. Turkse deelnemers hadden significant minder vaak cannabis gebruikt dan deelnemers

van de andere etnische groepen, maar de relatie tussen cannabis en schizofrenie was vergelijkbaar in alle etnische groepen.

In het laatste hoofdstuk vatten we de belangrijkste bevindingen van het proefschrift samen. De resultaten suggereren dat de verhoogde incidentie van schizofrenie en andere psychotische stoornissen bij eerste- en tweede-generatie immigranten begrepen kan worden door de sociale en culturele context waarin immigranten leven. De verhoogde incidentie lijkt bepaald te worden door factoren op verschillende niveaus, waaronder de wijk, de etnische groep, en het individu. In het bijzonder lijkt het risico op psychotische stoornissen te worden verhoogd door het behoren tot een etnische groep die een hoge mate van discriminatie ervaart, en door het hebben van een zwakke en negatieve identificatie met de eigen etnische groep. Deze factoren vertegenwoordigen mogelijk een situatie van chronische sociale stress, die schizofrenie zou kunnen veroorzaken bij individuen met een (genetische) predispositie voor de ziekte. Cannabis gebruik was een onafhankelijke risicofactor voor schizofrenie. Het was niet gecorreleerd met genetische predispositie voor de ziekte, maar was wel geassocieerd met ervaren discriminatie en een negatieve etnische identiteit. Dit suggereert dat cannabis gebruik een gevolg kan zijn van sociale stress.

Leven in een wijk met veel andere leden van iemands eigen etnische groep was geassocieerd met een lager risico op schizofrenie, evenals het hebben van een eenzijdige sterke oriëntatie op iemands eigen etnische groep (een gesepareerde identiteit). Deze factoren zouden sociale stress kunnen verminderen of voorkomen. Geconfronteerd met discriminatie en sociale tegenspoed lijkt het essentieel voor eerste- en tweede-generatie immigranten om een positieve identificatie met hun eigen etnische groep te behouden en om positief onderscheid te zoeken van de meerderheidsgroep.

De bevindingen hebben verschillende implicaties. De resultaten van dit proefschrift maken duidelijk dat de sociale context van belang is voor de aetiologie van schizofrenie. Verder onderzoek op dit gebied zou individuele factoren en contextuele factoren moeten integreren. Meer onderzoek is nodig om de relatie tussen ervaren discriminatie en schizofrenie te begrijpen, en om etnische identiteit en andere aspecten van sociale identiteit als risicofactoren van schizofrenie te bestuderen. Prospectieve studies zijn nodig om oorzaak en gevolg te onderscheiden. Bijvoorbeeld, etnische identiteit zou gemeten kunnen worden in personen met een hoog risico op schizofrenie, om te onderzoeken of transitie naar psychose wordt voorspeld door een zwakke en negatieve etnische identiteit. De invloed van beschermende factoren zoals hoge etnische dichtheid en sociaal kapitaal op de incidentie van schizofrenie zou verder onderzocht kunnen worden. Als sociale en culturele factoren inderdaad een causaal verband zouden blijken te hebben met schizofrenie, zou behandeling zich kunnen richten op het beïnvloeden

van deze factoren, en zouden preventieve strategieën kunnen ontwikkeld. Verscheidene suggesties voor behandeling en preventie worden gegeven.

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De schoenen uit, bedenken dat ik weer de verkeerde sokken aan heb, een schemerige trap op, een woonkamer in met een breedbeeld-televisie die hard aanstaat en ook niet uit gaat, met een Bollywood soap, Turks drama of Arabisch-klinkende muziek, prachtige meubels met veel glas en goudkleurige randen, of juist een lege, donkere kamer met een plastic zeiltje op tafel, lange banken langs de muren, foto's van Mekka of verre verwanten aan de muur, beeldjes van Vishnu of Shiva op het dressoir en veel zoete koekjes bij de thee...

O, o, Den Haag, mooie stad achter de duinen. Hoeveel uren heb ik niet rondgelopen in de Schildersbuurt, Transvaalkwartier, Laakkwartier en Spoorwijk, in Duindorp en Morgenstond. Soms op zoek naar onvindbare adressen, tevergeefs aanbellend bij donkere portieken, maar meestal hartelijk ontvangen door vriendelijke mensen. Eén keer proefde ik iets van wat het betekent om buitengesloten te zijn, toen iemand mij op straat in de Schilderswijk dreigend toeriep: "Jij hoort hier niet!"

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Het begon in 2001. De afdeling Eerste Psychose Behandeling (EPB) van Parnassia was nog niet zo lang geleden van start gegaan en ik mocht een vervolg geven aan het incidentieonderzoek dat Jean-Paul Selten en Natalie Veen eerder hadden gedaan. Elja van Maanen, sociaal-psychiatrisch verpleegkundige, zorgde ervoor dat de aanmeldingen bleven komen, dat familieleden werden geïnterviewd en dat de logistiek klopte. Dank je wel daarvoor, je hielp me de eerste stappen zetten. Bedankt Winfried Laan, psychiater bij de EPB, voor de ruimte die je gaf om onderzoek te doen, voor alle diagnostiekbesprekingen en voor alle discussies over het vak. Ik heb bewondering voor je kennis van vroege psychose, van diagnostiek en behandeling en voor de niet aflatende ijver waarmee je de patiënt altijd voorop stelt.

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Over de auteur

Wim Veling werd op 10 augustus 1974 geboren in Zwolle. In 1992 behaalde hij zijn VWO-diploma aan het Greijdanus college in Zwolle, en begon hij aan de studie Geneeskunde aan de Rijks Universiteit Leiden. In 1999 behaalde hij het artsexamen cum laude. Hij werkte een half jaar als arts-assistent tropengeneeskunde in het Kalabo District Hospital in Kalabo, Zambia. Van 2000-2001 werkte hij als arts-assistent psychiatrie bij de afdeling Sociale Psychiatrie van Riagg Rijnmond Noord-West in Rotterdam, en aansluitend bij een Transmuraal Zorg Team voor patiënten met schizofrenie bij Parnassia in Den Haag. In oktober 2001 startte hij de opleiding tot psychiater bij Parnassia Psycho-medisch Centrum (opleider prof.dr. H.W. Hoek) met een keuzejaar psychiatrische epidemiologie. In 2003 verkreeg hij een OOG-subsidie van ZonMw (Opleiding Onderzoekers in de GGZ). Hij behaalde in 2004 de graad Master of Epidemiology aan het Netherlands Institute for Health Sciences (Nihes) in Rotterdam. Sinds 2002 heeft hij gewerkt aan zijn promotieonderzoek, waarvan de bevindingen beschreven zijn in dit proefschrift. Dit onderzoek deed hij in nauwe samenwerking met de afdeling Eerste Psychose Behandeling van Parnassia, de afdeling Maatschappelijke Gezondheidszorg van het Erasmus Medisch Centrum in Rotterdam, en met de poliklinieken Interne Geneeskunde en Heelkunde van het Medisch Centrum Haaglanden in Den Haag. In het kader van het promotieonderzoek bracht hij in 2005 en 2006 werkbezoeken aan de afdeling Epidemiologie van de Columbia University in New York (afdelingshoofd prof.dr. E.S. Susser). Sinds oktober 2007 is hij bezig met het laatste jaar van zijn opleiding tot psychiater.

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