The Geography of Schizophrenia: Possible Links with Selenium and Calcium Deficiencies, Inadequate Exposure to Sunlight and Industrialization

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Introduction

According to Torrey (1980) schizophrenia was uncommon before 1800, but its incidence increased rapidly in both Europe and the United States during the nineteenth century. The disease is still uncommon in the Developing World, but as countries industrialize there is sometimes a sharp accompanying rise in schizophrenia. Prevalence rates also display at least an eightfold difference between long industrialized nations. The highest levels occur in Ireland, Scandinavia (especially portions of northern Sweden) and in Eastern Europe (particularly in Croatia). In parts of Western Ireland, for example, 1 out of 25 people will be afflicted during their lifetime. Intermediate prevalence rates occur in England, Germany, the United States and Japan. In the United States, for example, approximately one out of every hundred inhabitants eventually develops the disease. Southern Europe has a considerably lesser rate, although prevalence rates are hard to establish, probably because the illness is not a significant problem and there are conspicuously few data. This is also true of the Developing World, although Field (1960) found 41 schizophrenics amongst 4,283 Ashanti people in southern Ghana. Torrey (1980) considers that some of these individuals were misdiagnosed and postulates a prevalence rate of below 5 per thousand for the area.

Schizophrenia also appears to have socio-economic and racial dimensions. It occurs more commonly amongst the poor in the United States, England, Japan, Norway, Ireland and Iceland, but in India and possibly Italy it is apparently most frequent amongst the rich. The disease is also commonest amongst urban dwellers and blacks in the United States. Interestingly enough, in many countries, there is a known seasonality to the births of people who become schizophrenic, with the majority of them being born in the Winter and Spring (Torrey, 1980). It is also apparent that there is a genetic component to schizophrenia (Gottesman, Shield and Hanson, 1982). Siblings of schizophrenics have some 9 times the risk of developing the disease than do unrelated individuals (Shield, 1975).

Method

Attempts to discover links between schizophrenia and geographical factors require both synchronous environmental and medical data from the same spatial units. Since data of both kinds is available from the United States, this was considered to be a viable area for a preliminary study. The author's environmental data bank has been described in considerable detail elsewhere (Foster, 1986). The best source of information on the geographical distribution of schizophrenia in the United States is the annual survey of *Patients in Mental Institutions*, conducted by the Biometry Branch of the Office of Program Planning and Evaluation, National Institute of Mental Health. These volumes enumerate patients in state and county mental hospitals and private and general hospitals that provide psychiatric care. Since much of the environmental information had been collected in the 1960s, it was decided to use medical data from 1965. Unfortunately, information from state and county mental institutions was not

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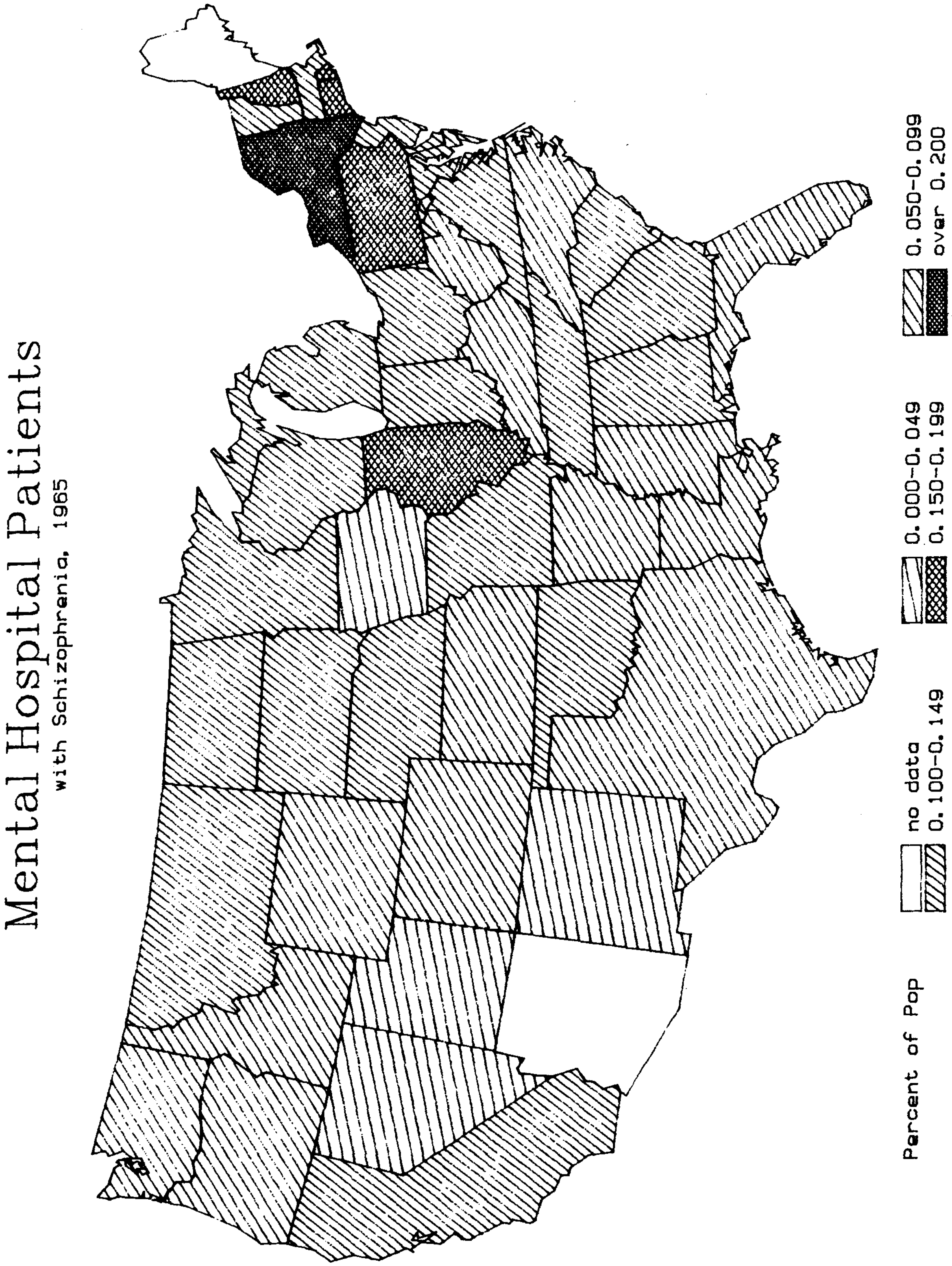
Figure 1


Mental Hospital Patients
with Schizophrenia, 1965
Percent of Pop
no data
0.100-0.149
0.000-0.049
0.150-0.199
0.050-0.099
over 0.200

compatible with that from private and general hospitals. Whilst details of the number of patients being treated for schizophrenic reactions at the end of 1965 were given for 272 state and county mental hospitals, other institutions reported only admission and discharge rates for schizophrenics. Initial analysis, therefore, was restricted to schizophrenic patients in state and county mental facilities, many of these requiring long term care. Figure 1 illustrates the spatial distribution of such individuals. The data used to produce this illustration was obtained by dividing the number of patients recorded from each state by the total population of that state, as established by the 1960 census. It appears obvious from this figure that prevalence rates are particularly high in the northeastern United States.

Whilst such visual impressions are interesting, techniques of analysis are required to establish the extent and nature of relationships between schizophrenia, the dependent variable, and one or more explanatory or independent variables. In the current study, Pearson correlation coefficients and stepwise multiple regression analysis were used, respectively, for this purpose. What is needed is some knowledge about how the average variation in schizophrenia is associated with change in an independent variable, or variables, for example, the levels of copper or lead in soils. Both Pearson correlation and stepwise multiple regression provide such an understanding of possible causal links between variables. The former technique, however, is restricted to the examination of associations between only two variables; multiple regression is not.

Results

It was found that the prevalence of schizophrenia in state and county mental hospitals in 1965 showed the strongest positive correlation with selenium deficient fodder crops ($r = 0.58497$, $p = 0.0001$). In contrast, the highest negative correlation occurred between schizophrenia and sunlight ($r = -0.57024$, $p = 0.0001$). There were also several strong positive correlations with evidence of industrial activity, namely the proportion of the population employed in manufacturing ($r = 0.55393$); industrial water withdrawal ($r = 0.54871$), the population density of the state ($r =0.53936$), the number of toxic waste sites per unit area ($r = 0.51000$, $p = 0.0003$) and the use of road salt ($r = 0.50225$, $p = 0.0004$) ($p = 0.0001$ unless otherwise stated). Also of note appeared to be the fairly strong negative correlations with soils that contained very high levels of calcium ($r = -0.45784$, $p = 0.0014$) and were enriched in strontium ($r = -0.43360$, $p = 0.0026$). All variables that were found to be significant at the 0.01 level are given in Table 1.

Using the same data set schizophrenia was also subjected to stepwise multiple regression. In this method of analysis the first variable entered is the one with the highest linear correlation with the dependent variable (schizophrenia). The standardized partial regression coefficients of the other independent variables are then examined and the one having the highest coefficient is added to the regression equation. Each time that a variable is added to the equation, the other variables in it are tested for significance at the 0.01 level. Those found not to account for significant reductions in the variance of the dependent variable are deleted. This procedure continues until all variables in the equation are significant and those outside are not (Tidball and Sauer, 1975).

Stepwise multiple regression, for example, produced the following two variable model which could explain 52.5% of the variance involved in the distribution of patients suffering from schizophrenia in state and county hospitals in 1965.

$$\text{Schizophrenia} = 0.0560 + (0.00655 \text{ X En5}) + (0.00101 \text{ X PL Cr})$$

Where: En5 is the proportion of the state in which at least 80 percent of the fodder crops contain less than 0.10 ppm selenium. PL Cr is the percentage of the state with low soil chronium levels.

The final model produced by stepwise multiple regression contained six variables and could explain 82.5% of the variance involved in the distribution of schizophrenic hospital patients in 1965.

Schizophrenia = 0.185 +
(0.00000476 X En3) - (0.000419 En 15) +
(0.198 Enl3) +(0.00112 PL Cr) +
(0.000675 PL Pb) + (0.000622 PL K)

Where: En3 is the population of the state. Enl5 is the annual sunlight. Enl3 is the DDT concentration used on crops. PL Cr is the percentage of the state with low soil chromium levels. PL Pb is the percentage of the state with low soil lead levels and PL K is the percentage of the state with low soil potassium levels.

Conclusions

Obviously, because of the limitations of the medical data used in these analyses, any conclusions must be very tentative. Indeed, correlations in themselves can never prove causal relationships beyond doubt. The author is fully aware that much more research is necessary to test the validity of any hypotheses based on such associations. Nevertheless, the correlations presented in Table 1 and in the stepwise multiple regressions are intriguing, since they tend to hint at possible reasons for historical change in the incidence of schizophrenia and for its current world distribution patterns.

It has been suggested that the biological defect in schizophrenia may be related to excess dopamine activity, to the production of an abnormal opioid, or excessive amounts of a normal opioid, or to hypersensitivity to wheat proteins. It has also been hypothesized that the disease may be associated with prostaglandin deficiency, to an allergic phenomenon, to an inability to metabolize zinc effectively, or to pineal deficiency. Horrobin (1979) has suggested that these various hypotheses are not mutually exclusive, but may represent different dimensions of the same problem. The final common path in schizophrenia, he suggests, may be a failure of the formation and action of prostaglandins of the 1 series. Interestingly enough, the strongest correlation shown in Table 1 is between the prevalence of schizophrenia in the United States and low levels of selenium entering the food chain (r = 0.58497, p = 0.0001). Vincent (1970) has suggested that a dietary selenium deficiency results in the inability of the human body to manufacture several prostaglandins. Production of prostaglandin E_2 and A_2, for example, are both diminished. This appears to occur because a selenium-containing enzyme is necessary in their manufacture and perhaps for that of other prostaglandins (Passwater, 1980). The significance of selenium in schizophrenia is also hinted at by the moderate negative correlation of the disease with soils containing very low levels of mercury (-0.38624, p = 0.0080). Mercury is antagonistic with selenium and tends to reduce its biological availability (Foster, 1986). For this reason, soils very low in mercury are likely to produce crops and livestock with higher selenium content. Whether calcium and strontium play any direct role in schizophrenia is unknown, but it is well established that selenium is most soluble in alkaline soils (Passwater, 1980). This might explain the negative correlations between soils that are very high in these elements and schizophrenia. Other correlations in Table 1 also appear worthy of further examination. The strong negative association with sunlight (r = -0.57024, p = 0.0001), for example, might be invoked to explain why the disease is so common in the higher latitudes of the Northern Hemisphere. In contrast, strong sunlight may be partially responsible for the lower prevalence of schizophrenia in southern Europe and the Developing World; the latter being mainly tropical and equatorial. In addition, it is possible that lack of exposure of expectant mothers to adequate sunlight might be associated, in some way, with the greater frequency of winter and spring birth dates amongst schizophrenics. Why sunlight might be significant in this way is unknown. However, the recent recognition of SAD, seasonal affective disorder, which is characterized by severe seasonal mood swings, illustrates that sunlight may be directly related to mental health (Toufexis, 1988). Alternatively, since sunlight is required by the body to produce vitamin D, schizophrenia may in some way be linked to deficiencies of this vitamin, either prior to birth or later in life. The moderate negative correlation between schizophrenia and soils that are very high in calcium (r = -0.45784, p = 0.0014) also appears to hint at a vitamin D connection, since this vitamin

TABLE 1
Associations Between Schizophrenia and Environmental Variables

Environmental Variable	Correlation Coefficient	Level of Significance
Low selenium content in fodder crops	0.58497	0.0001
Annual sunlight	-0.57024	0.0001
Proportion of population employed in manufacturing	0.55393	0.0001
Industrial water withdrawals (volume divided by land area of the state)	0.54871	0.0001
Population density	0.53936	0.0001
Toxic waste site density (number of Superfund sites divided by land area of state)	0.51000	0.0003
Road salt use (Tonnage divided by land area)	0.50225	0.0004
Population of the state	0.47566	0.0008
Very high soil calcium	-0.45784	0.0014
Egg production	0.45431	0.0015
Percentage of state disturbed by sand and gravel mining	0.43588	0.0025
Very high soil strontium	-0.43360	0.0026
Rural water withdrawals (volume divided by land area of the state)	0.42135	0.0035
Land area of the state (excluding lakes)	-0.41719	0.0039
Total area of the state	-0.41595	0.0040
Very low soil mercury	-0.38624	0.0080
Summer air pollution (suspended particulates)	0.38510	0.0082
Dieldrin pollution	0.38011	0.0092
Very high soil sodium	-0.37634	0.0099

is necessary for the optimal use of calcium (Kirschmann and Dunne, 1984).

At least eight of the variables with the highest positive correlations with schizophrenia are indicators of industrialization. Clearly schizophrenia is particularly common in heavy manufacturing states. This tends to confirm Torrey's (1980) hypothesis that the disease is essentially one of civilization. Why high schizophrenia prevalence may be related to manufacturing is unclear, but several hypotheses seem obvious. Firstly, some pollutant or group of pollutants may be involved. Secondly, industrialization generally results in less exposure to sunlight, as a consequence of more indoor work and shade from tall buildings. Thirdly, it is associated with major changes in diet and the greater consumption of refined, processed and canned foods, that is with alterations in the intake of various minerals and vitamins. Such a decline in the consumption of fresh foods may have various mental health related implications (Hoffer and Walker, 1978). Of course, industrialization is also associated with enormous political, social and economic changes which may influence the prevalence of the disease.

Although the preceding discussion is essentially speculation, it does indicate that correlations between geographical variables and the prevalence of schizophrenia are worthy of more detailed examination. Hopefully, further research at the county or larger scale in the United States and elsewhere, covering longer time periods, will provide additional directions for medical research.

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