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A prevalence estimate of pervasive developmental disorder among Immigrants to Israel and Israeli natives

A file review study

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Abstract *Background* The prevalence rates of pervasive developmental disorder (PDD) have risen in the West over the last 10 years. There is argument over the etiology of this change in rates. Social and cultural processes including migration have been hypothesized. Israel, as a country of ongoing immigration with a national registry of children diagnosed with PDD, offers an opportunity to compare rates of PDD among immigrants from developing countries and native Israelis. *Method* A Social Security national registry of 1,004 children diagnosed with PDD was reviewed and rates were calculated using data extracted from the Israel National Bureau of Statistics. Of all Jewish children that were born in the years 1983–1997 and who are currently living in Israel, we defined four groups: (1) native Israelis of non-Ethiopian extraction (N = 1,198, 300), (2) native Israelis of Ethiopian extraction (N = 15,600), (3) immigrants of non-Ethiopian extraction (N = 110,300) and (4) children born in Ethiopia (N = 11,800). A further breakdown of groups 1 and 3 by well-characterized ethnic or geographical origins was not possible. *Results* The rate of PDD was significantly elevated in native Israelis as compared to all immigrant children. Among immigrants, the rate of PDD in Ethiopian-born children was lower than that of those born in other countries. The rate of PDD in immigrant Ethiopian children was much lower than in native Israeli children of Ethiopian extraction. *Conclusions* Birth in Israel, an industrialized country, is a marker for an environmental risk factor for PDD. This may indicate that gestation, birth or infancy in industrialized countries exposes children to environmental insults that increase the risk for contracting PDD.

Key words PDD – autism – immigration – prevalence rate – risk factor.

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Introduction

Pervasive Developmental Disorders (PDD) include autism, Rett's disorder, childhood disintegrative disorder, Asperger's syndrome and pervasive developmental disorder not otherwise specified [1]. According to Israeli law, a child diagnosed with PDD qualifies for special needs funding. For this reason there is a national registry of children diagnosed with PDD. Within the disorders grouped as PDD, autism is the most common [2, 3], accounting for about half of the children within the PDD group [4]. The prevalence of PDD in Western Europe and the United States is over 20 children per 10.000 [2, 5–7]. A comparable rate of 10/10.000 was found for autism in the Haifa region of Israel [8] with a boy:girl ratio of 4:1. A weighted national rate of 8/10.000 for the whole of Israel was estimated [9]. Research on the rate of PDD and/or autism in immigrants and in their countries of origin has yielded conflicting results. Some studies have found a higher rate of PDD and/or autism in immigrants than in the populations into which they emigrated [10, 11]. Other studies have found a lower rate of PDD in immigrants compared to natives of Western Europe [12–14]. Small samples and lack of uniform diagnostic procedures are impediments to generalizing the results of these studies and understanding the impact of immigration on the risk for PDD. The current study used a national registry of diagnosed PDD as well as major waves of immigration to Israel from Ethiopia and elsewhere to address this question.

SPPE 696

Subjects and methods

Study population

The demographic data included the entire Jewish population in Israel born between 1983 and 1997. The data on children diagnosed with PDD were compiled from:

1. A registry of all children born within this 14-year period diagnosed with PDD and registered by the Israel Social Security Service for receiving disability support, compiled by Senecky et al. [9].
2. Children of Ethiopian extraction were identified through their family names, which are the father's given name. For reasons of patient privacy, the families were not approached directly. All 85 names that were identified as certainly Ethiopian, probably Ethiopian or possibly Ethiopian were reviewed by three Ethiopian experts blind to the aims and hypotheses of the current study. Two of the experts were familiar with the Gondar and the Tigre regions of Ethiopia, languages and naming traditions. The third was of Tigre extraction and an expert on Tigre language and naming traditions. Thirteen names agreed upon by all three to be Ethiopian were included in the count as children of Ethiopian extraction. Names about which there was disagreement among the three experts were checked against a central database and shown to be non-Ethiopian.
3. National data on children born in Israel between 1983 and 1997 were obtained from the Israel National Bureau of Statistics [15]. These data were used for the nominators of the prevalence estimates calculated. The identification of the four groups for the nominators by country of birth (Israel, Ethiopia, countries other than Ethiopia) was directly available from the demographic tables [15]. Children born in Israel of non-Ethiopian parents cannot be identified by country of origin because of admixture of immigrant groups in Israel. Groups 2 and 4 can be identified because of the severe endogamy practiced by the Ethiopian Jewish community. The four groups identified were:
   (1) Native Israelis of non-Ethiopian extraction (N = 1,198,300).
   (2) Native Israelis of Ethiopian extraction (N = 15,600).
   (3) Immigrants of non-Ethiopian extraction (N = 110,300).
   (4) Children born in Ethiopia (N = 11,800).

Results

The prevalence estimates for PDD in the different groups of children fell between 9.0/10.000 children for Israeli-born non-Ethiopian children and 0.0/10.000 for first-generation Ethiopian children. Significant differences in prevalence were found between Israeli-born children and immigrant children. Native Israelis had a higher PDD prevalence rate than all those born abroad: $Chi^2 = 22.4$, df = 1, p = 0.000, OR = 1.85 (95 % CI 1.5–2.4). Non-Ethiopian children born in Israel were significantly elevated in PDD relative to Israeli-born Ethiopian children: $Chi^2 = 15.6$, df = 1, p = 0.000, OR = 1.7 (95 % CI 1.3–2.2). There were no immigrant children born in Ethiopia who were diagnosed with PDD. Non-Ethiopian immigrant children were significantly elevated in their PDD prevalence rate relative to Ethiopian children: $Chi^2 = 6.3$, df = 1, p = 0.01, OR = incalculable. Second-generation Ethiopian children had higher PDD prevalence rates than first-generation Ethiopian children, $Chi^2 = 9.8$, df = 1, p = 0.002, OR = incalculable. The boy:girl ratio of Ethiopian children with PDD was 1.6, and of non-Ethiopians 3.8. The sex ratios were not significantly different. The prevalence rates for all groups are shown in Table 1.

Discussion

The current study found that the rate of PDD in children born between 1983 and 1997 in Israel was significantly elevated compared to that of children who immigrated to Israel. This result held when controlling for ethnicity, comparing first- and second-generation Ethiopian children. The lowest prevalence rate was found for first-generation Ethiopian children, and this rate was also significantly lower from that of other immigrant children.

The elevated risk for Israeli-born Ethiopian children vs. Ethiopian-born children living in Israel

Ethiopian children born in Israel had a higher rate of PDD compared to native-Israeli children of Ethiopian extraction. This result should be considered in the context of the Ethiopian community and its immigration history. As a result of immigration and natural growth, about 85.000 Ethiopian Jews live in Israel, and only a handful of the community remain in Ethiopia. Ethiopian Jews were transported to Israel in two main waves: "Operation Moses" from 1984 to 1985 (6,700 immigrants) and "Operation Solomon" in 1991 (over 14,000 immigrants). The remaining immigrants arrived in a series of smaller waves [16]. The process of immigration was fraught with hardship and mortal danger [16]. Although no restraints were placed on entry to Israel, the process of immigration was so stressful that it was, in effect, selective for youth, health and fitness [16].

The Ethiopian community in Israel is comparatively young, more than 50 % are 18 years of age or under. Over a quarter of today's Ethiopian community was born in Israel. The birth rate of around 30 per 1,000 is about 50 %

Table 1 Number of children and prevalence estimates of PDD in native Israelis and in immigrants

	Born abroad			Israel-born		
	Ethiopian	Other	Total	Ethiopian	Other	Total
PDD	0	59	59	13	991	1,004
Total	11,800	110,300	122,100	15,600	1,098,300	1,113,900
Rate/10,000	0	5.3	4.8	8.3	9.0	9.0
SE	0	0.7	0.6	0.2	0.3	0.3

higher than that found among the general Israeli population. There is hardly any intermarriage between Jews of Ethiopian extraction and Jews of other ethnic and geographical extraction; thus, the Ethiopian Jews at this time are a distinct group [16]. In Ethiopia and after immigration to Israel, a strong and consistent taboo on inbreeding is enforced. Before a marriage in the Ethiopian community is approved records are examined and seven generations of no common kin are observed [16].

Most of the Ethiopian Jews who immigrated to Israel came from traditional-agricultural villages in the Gondar and Tigre regions in Northern Ethiopia. The rapid natural growth of the Ethiopian Jewish community in Israel made it possible to compare the rates of PDD in groups of first- and second-generation Ethiopian children who shared cultural and ethnic characteristics. Those born in Ethiopia went through embryonic and postnatal early development in traditional agricultural surroundings, while those born in Israel were exposed to a more industrialized and urban environment from conception.

There are no epidemiological data for PDD in Ethiopia. There is anecdotal evidence from child psychiatrists in Addis Ababa (personal communication) that there are cases of autism and PDD in Ethiopia, but no estimate of their prevalence rate. Thus, our results of no Ethiopian-born children living in Israel diagnosed with PDD and 8.3/10.000 born in Israel of Ethiopian extraction may be due to low initial rates in Ethiopia and to natural selection in the process of immigration. They cannot be due to genetic factors because of the strength of endogamy within Ethiopian Jews [16] coupled with the taboo on inbreeding. They may be due to an environmental effect on early development in Israel not found in Ethiopia.

The elevation of PDD in native Israelis compared to all immigrant children

The current study found that there was an elevation of PDD in Israeli natives relative to all immigrant children. This result held also when only non-Ethiopian immigrants were considered. A possible explanation for the difference in rates is that there was under-diagnosis of PDD in children born abroad and living in Israel. A recent study of PDD in the United States [17] of children diagnosed and treated for autism by Medicaid found that the mean age at diagnosis of black children was higher than that of white children. Mandell et al. [17] related these results to differences in help-seeking, advocacy and support, as well as to clinical behaviors. Immigrants to Israel are the focus of concerted professional efforts and are regularly monitored by medical staff and, thus, severe disorders, including PDD, are not likely to be overlooked. Under-diagnosis is unlikely, but misdiagnosis is a possibility. A recent study in California [18] compared the secular trends in rates of autism and mental retardation in different population groups and found that immigrants were not different from Californian-born groups. However, the same group [19] found that, while the rate of diagnosed autism had risen in California over the last decade, rates of mental retardation without autism had dropped, suggesting that the increase of diagnosis of autism is a result of growing appreciation for the comorbidity of autism and mental retardation, and better screening practices of mentally retarded children for autism. Since the current study was limited in that it did not compare the rates of PDD and of mental retardation, one possible explanation of the difference in rates is that, in Israel, immigrant children may be more likely to be diagnosed with mental retardation and not PDD if they are comorbid for both conditions.

The elevation of PDD in immigrants from other countries compared to Ethiopian immigrant children

Immigrants from all countries other than Ethiopia were estimated to have an elevated prevalence rate of PDD relative to immigrants from Ethiopia. There are three competing explanations that come to mind. The first is that the phenomenon of under-diagnosis of PDD is more severe among the Ethiopians who have more difficulty communicating with the medical professionals than immigrants from more Western cultures [20]. The second is that the harshness of the escape from Ethiopia and immigration to Israel was more selective than the challenge of emigrating from other countries to Israel and, thus, there was more selection against Ethiopian-born infants and children with PDD. The third is that other countries of origin, a mixed bag, include on average a greater dose of whatever industrial environmental risk factor we hypothesize than does rural Ethiopia.

Nature and nurture in the etiology of PDD

Although no studies have examined genetic causes for PDD, considerable research has focused on genetic influence on autism, the most common disorder included within the PDD diagnostic range. Twin and family studies [21] estimated heritability in excess of 90% for autism. More recently, studies have shown an overall excess of twins both identical and fraternal with autism among affected sib-pairs, suggesting that former heritability estimates may have been inflated [22]. A growing appreciation for the complexity of autism inheritance has accompanied the growing body of research. When genetic research on autism began, a single gene was suspected. Current hypotheses attribute the genetic variance to up to 20 genes [23]. In any event, for autism, and even more so for PDD, genetic factors alone do not account for all the variance observed, and environmental factors also contribute.

Behavior genetics has shown that, while environmental factors contribute to the etiology of complex

phenotypes, it is usually unique, and not common, familial environmental influences that affect individual differences in phenotype [24]. However, behavior genetics has been less than successful in identifying specific environmental factors, common or unique, that contribute to individual differences in behavioral phenotypes. There has been evidence that exposure to certain toxins early in embryological development might increase the risk for autism [25] although not for the wider phenotype. There is evidence that autism is accompanied by activation of inflammatory response in the immune system, suggesting that infectious factors are involved [26]. Risk associated with the inoculations against measles-mumps-rubella has been hypothesized as an agent for causing much of the rise in autism rates [27]. While this hypothesis has not been supported by rigorous epidemiological work [28], there is a lingering doubt about the source of the rise in autism. Many families have not allowed younger siblings of an autistic child to be inoculated, thus making the inference about the contribution of the inoculation to the risk more difficult [28]. Although the environmental and or genetic risk factors must be mediated by subtle CNS damage in structure or function, neurological studies have not yet identified the damage associated with PDD in a way that clarifies the etiology.

The elevated rates of PDD in Israeli-born children vs. non-Israeli-born children living in Israel, and even more so the elevated rate of PDD in second-generation vs. first-generation Ethiopian children suggest that there is an important environmental influence on the risk for PDD in Israel. Moreover, environmental contaminants of some kind associated with the urban, industrialized lifestyle, prevalent in most of Europe and the United States, and increasingly in other parts of the world, may be at fault for the rise in rates of autism and PDD in other countries.

Limitations

A limitation of this study was that it did not begin in Ethiopia and other countries of origin by estimating the prevalence of PDD in the original communities. This limitation is not easily overcome as most immigrants migrate in response to profound political, military or economic changes in their country of origin, which make a prevalence study there very difficult.

An additional limitation is that this is a file review study and, thus, calculates the rates of the children diagnosed and treated for PDD, rather than directly sampling the population and testing children for the disorder. The results are, thus, possibly confounded because prevalence was indistinguishable from recognition by social security.

Conclusion

Selective immigration and under- or mis-diagnosis of PDD and autism are unlikely to be the causes of the rate differences found between Israeli-born and immigrant children living in Israel. It seems more likely that birth in Israel is a marker for some environmental risk factor associated with industrialization and urbanization. However, rigorous prospective research is needed in order to conclusively confirm this hypothesis. The current study shows the possibility of a non-genetic, environmental risk factor. Further research, identifying specific risk factors, would be useful for understanding the causal factors for PDD and, in the long run, for treatment and prevention.

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