

Parental migration and Asperger's syndrome

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Abstract Parental immigration has been suggested as a possible risk factor for autism spectrum disorders (ASD), but findings have been inconsistent. Very few studies have focused specifically on Asperger's syndrome. The aim of this study was to examine the association between maternal and paternal immigration and the diagnosis of Asperger's syndrome in offspring. The study was a nested case–control study based on a national birth cohort in Finland. Children born in 1987–2005 and diagnosed with Asperger's syndrome by the year 2007 were identified from the Finnish Hospital Discharge Register ($N = 1,783$). Four matched controls for each case were selected from the Finnish Medical Birth Register ($N = 7,106$). Information on maternal and paternal country of birth and mother tongue was collected from the Finnish Central Population Register. The study showed that children whose parents are both immigrants have a significantly lower likelihood of being

diagnosed with Asperger's syndrome than those with two Finnish parents [adjusted odds ratio (aOR) 0.2, 95 % confidence interval (CI) 0.1–0.4]. No significant associations were found between having only one immigrant parent and the diagnosis of Asperger's syndrome. A regional analysis showed a significantly decreased likelihood of the diagnosis of Asperger's syndrome in children whose mother (aOR 0.1, 95 % CI 0.01–0.5) or father (aOR 0.2, 95 % CI 0.05–0.5) was born in Sub-Saharan Africa. The findings may help in identifying risk factors for different ASD subtypes. On the other hand, they might reflect service use of immigrant families in Finland.

Keywords Autism · Asperger's syndrome · Risk factor · Parental · Migration

Introduction

Autism spectrum disorders (ASD) are a group of developmental disorders characterized by impaired social interaction and communication and by restricted, stereotyped and repetitive patterns of behavior. The International Classification of Diseases (ICD) divides ASD into several subtypes, of which the most common are childhood autism, Asperger's syndrome and pervasive developmental disorder not otherwise specified (PDD-NOS). Asperger's syndrome can be distinguished from childhood autism mainly by the absence of significant delay in language and cognitive development. It is commonly considered to be a milder form of autism. The diagnostic criteria for ASD were previously very similar in the Diagnostic and Statistical Manual of Mental Disorders (DSM), although the most recent version (DSM-5) has a single umbrella diagnosis instead of separate disorders. The prevalence of ASD

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has been steadily increasing and it has been estimated that the current median prevalence is 0.62–0.70 % globally [1]. This increase highlights the importance of understanding the contexts of diagnosis. Suggested explanations for the increase include changes in diagnostic concepts and practices, increased awareness, younger age at diagnosis and change in the distribution of risk factors [1, 2].

The etiology of ASD is known to involve both genetic and environmental factors [3–5]. An often-mentioned risk factor is parental migration, which may reflect either environmental risk factors in the country of origin or in the host country or genetic factors. Suggested mechanisms include increased maternal stress, poor nutrition and exposure to novel viruses and intrauterine infections [6–8], but they remain unstudied. A popular hypothesis is that the increased risk of ASD is related to the decreased level of vitamin D among parents who have dark skin and have migrated north, because the lack of vitamin D might be associated with ASD in offspring [9–11].

Several European studies have shown that having a mother born outside Europe is associated with an increased risk of ASD [7] or childhood autism [12–14] in offspring. Similarly, an Australian study showed that having an immigrant mother increases the risk of ASD [8]. There are also studies of populations from Europe and the United States in which maternal immigration has not been associated with an increased risk of ASD [15, 16] or childhood autism [17, 18] in offspring. The studies on paternal immigration have shown inconsistent results as well [15–17, 19]. A study based on the Finnish Prenatal Study of Autism (FIPS-A) showed that in Finland, having an immigrant mother or two immigrant parents is associated with an increased risk of childhood autism in offspring [20]. A regional analysis showed that the risk was increased for those with a mother born in the former Soviet Union or Yugoslavia and for those with a mother or a father born in Asia [20]. No other Finnish studies have been conducted, which may be related to the relatively small number of immigrants. This number is, however, increasing. In 2012 the proportion of foreign-born people in the Finnish population was 5.3 % [21].

To our knowledge, only one previous study has examined Asperger's syndrome in relation to migration separately from other ASDs. The study was conducted in Sweden and showed that having a mother born outside Nordic countries was positively associated with childhood autism, but on the contrary, negatively associated with Asperger's syndrome [13]. In a Dutch study, Asperger's syndrome was analyzed together with PDD-NOS [16]. It showed that children whose parents were born in developing countries had a decreased risk of Asperger's syndrome or PDD-NOS. The direction of association between parental immigration and childhood autism was opposite, although it was not statistically significant. Each study was limited in small sample

size and covered a small geographical region. In a large nationwide Swedish study diagnostic subtypes of ASD were not examined separately, but it was shown that maternal immigration was associated only with increased risk of low-functioning ASD, which was defined as ASD with comorbid intellectual disability [6].

The aim of this study was to examine the association of maternal and paternal immigration with Asperger's syndrome in offspring in Finland.

Methods

The study is based on the FIPS-A. It is a national case–control study that aims to identify risk factors for ASD. The methods have been described in detail by Lampi et al. [22]. The study was authorized by the Ministry of Social Affairs and Health of Finland (STM/2593/2008) with approvals from the National Institute for Health and Welfare (THL), the Ethics Committee of the Intermunicipal Hospital District of Southwest Finland, and the Institutional Review Board of the New York State Psychiatric Institute. To assess the association between parental migration and Asperger's syndrome, a linkage was conducted between three national registers for 1,783 cases and their 7,106 matched controls born in 1987–2005.

Case and control identification

Of all children born in Finland in 1987–2005, those diagnosed with Asperger's syndrome by the year 2007 were identified from the Finnish Hospital Discharge Register (FHDR), a nationwide register maintained by THL. The diagnoses included in the register are based on the ICD. In this study, the ICD-10 code F84.5 on Asperger's syndrome was used for identification. The register includes the personal identification numbers, which can be used for linkage with other registers. In Finland, children suspected to have Asperger's syndrome are generally referred from primary health services to specialized units which are placed in public hospitals and include both inpatient and outpatient services. They are assessed by a multiprofessional team using standardized methods and diagnosed by a child neurologist or psychiatrist. The FHDR includes information on all inpatient care for the whole follow-up period and information on outpatient visits in specialized services since 1998.

Four controls per case were selected from the Finnish Medical Birth Register (FMBR). It is a national register maintained by THL and includes information on maternal background, pregnancy, and the prenatal and neonatal period up to age 7 days on all births in Finland. The register includes mothers' personal identification numbers linked to

children. The controls were matched to each case by date of birth (± 30 days), region of birth, sex, and residence in Finland. The exclusion criteria for controls were ASD or severe/profound mental retardation according to the FHDR. Of the originally matched 7,132 controls, 26 had invalid or incomplete personal identification numbers for the mother or child, and were removed. The final number of controls was thus 7,106.

Parental immigration status

The data on parental country of birth and mother tongue were collected from the Finnish Central Population Register (CPR), which is a national register that contains basic information about Finnish citizens and permanent residents in Finland. Personal identification numbers are issued at birth or at migration. Asylum seekers and recent migrants without personal identification numbers are not included in the register. Biological parents are linked to their children with their personal identification numbers in the CPR. First-generation immigrant parents were defined as those who were born abroad and whose mother tongue is not Finnish. Those who were born in Finland and/or whose mother tongue is Finnish were defined as Finnish.

Two different methods were used for classifying parents. First, a four-category variable was used for the primary analysis: both parents Finnish (reference), mother

immigrant and father Finnish, father immigrant and mother Finnish and both parents immigrants. Second, a regional analysis was conducted separately for mothers and fathers using the following categorization: (1) Finnish (reference), (2) Western countries (most European countries, North America, Australia and New Zealand), (3) Countries which were part of the former Soviet Union or Yugoslavia, (4) Sub-Saharan Africa, (5) North Africa and the Middle East, and (6) Asia (excluding the Middle East). The categorization was based on geographic and socioeconomic factors. All “Western countries” are members of OECD (Organization for Economic Co-operation and Development) except for Romania and Bulgaria, which are nevertheless members of the European Union.

Covariates

The inclusion of covariates was based on analyses of bivariate associations between: (1) selected variables from the FMBR or CPR and Asperger’s syndrome, and (2) these same variables and parents’ immigration status among controls. The results of these analyses are shown in Table 1. Maternal age, maternal smoking during pregnancy and parity were associated with both the exposure and the outcome ($p < 0.1$), and they were included in the adjusted analysis.

Maternal socioeconomic status (SES) was included as a covariate in an additional analysis only, because its use has some limitations. This four-category variable is based

Table 1 Covariates in relation to immigration status in controls and in relation to the risk of Asperger’s syndrome

Covariates	Immigration				<i>p</i> value ^f	Relationship between covariates and Asperger’s syndrome, <i>p</i> value ^f
	Both parents Finnish <i>n</i> (%)	Mother immigrant <i>n</i> (%)	Father immigrant <i>n</i> (%)	Both parents immigrants <i>n</i> (%)		
Maternal age (\geq median, 29 years)	3,729 (55.2)	44 (50.0)	73 (54.9)	51 (38.4)	0.001	0.07
mean (SD) (years)	29.4 (5.1)	29.4 (4.8)	29.6 (5.1)	27.2 (4.9)		
Paternal age (\geq median, 31 years) ^a	3,171 (47.0)	49 (55.7)	59 (44.3)	73 (54.9)	0.10	0.87
mean (SD) (years)	31.7 (5.8)	34.7 (8.4)	31.9 (7.3)	32.4 (6.2)		
Maternal smoking ^b	1,047 (15.9)	8 (9.4)	20 (15.5)	6 (4.8)	0.003	0.04
Previous births (≥ 2) ^c	1,658 (24.6)	16 (18.2)	19 (14.3)	48 (36.1)	<0.001	<0.0001
Preterm birth (<37 weeks) ^d	332 (4.9)	5 (5.7)	10 (7.5)	10 (7.5)	0.29	0.08
Low birth weight (<2,500 g) ^e	185 (2.7)	5 (5.7)	7 (5.3)	10 (7.5)	0.001	0.38
mean (SD) (g)	3,614 (541)	3,482 (524)	3,482 (557)	3,419 (602)		

^a frequency missing = 39 cases and 91 controls

^b frequency missing = 48 cases and 155 controls

^c frequency missing = 14 cases and 43 controls

^d frequency missing = 12 cases and 42 controls

^e frequency missing = 7 cases and 29 controls

^f χ^2 test

Table 2 Immigration status by Asperger's syndrome in cases and controls

	Cases <i>n</i> (%)	Controls <i>n</i> (%)	OR (95 % CI)	<i>p</i>	Adjusted ^a OR (95 % CI)	<i>p</i>
Both parents Finnish	1,719 (96.4)	6,752 (95.0)	Ref.		Ref.	
Mother immigrant	23 (1.3)	88 (1.2)	1.0 (0.6–1.6)	0.93	1.1 (0.7–1.7)	0.75
Father immigrant	35 (2.0)	133 (1.9)	1.0 (0.7–1.5)	0.89	1.0 (0.7–1.4)	0.91
Both parents immigrants	6 (0.3)	133 (1.9)	0.2 (0.1–0.4)	<0.0001	0.2 (0.1–0.4)	0.0001

OR odds ratio, CI confidence interval

^a Adjusted for maternal age, maternal smoking and parity

primarily on maternal occupation during pregnancy. The categories are as follows: upper white collar workers, lower white collar workers, blue collar workers and “others”, including for example students, housewives and entrepreneurs. The variable has been included in the FMBR since October 1990 and therefore the data are not available for births occurring before that date. In addition, it is considered to be unreliable in refugee populations, because information on their education is incomplete and many of them are outside the labor force, e.g. in school or not employed. No information on paternal SES was available.

Statistical analysis

The association between parental immigration and Asperger's syndrome was quantified by calculating odds ratios with 95 % confidence intervals using conditional logistic regression analysis and two different classifications for parental immigration, as explained above. The reference group in each analysis was “Finnish parents”. Maternal age, maternal smoking during pregnancy and parity were included in adjusted analyses. Age at diagnosis among children of Finnish parents and three different groups of immigrant parents were compared using analysis of variance (ANOVA, *F* test). To avoid multiplicity, the *p* values were Bonferroni-corrected. A *p* value of less than 0.05 was considered statistically significant. Statistical analyses were performed with SAS software (SAS 9.4, SAS Institute, Cary, NC, USA).

Results

The relationships between the covariates and immigration among the controls as well as between the covariates and Asperger's syndrome are shown in Table 1. Maternal age above the median was more common in families with two Finnish parents or with an immigrant father than in other families. Paternal age above the median was most common in families with two immigrant parents or an immigrant mother. Maternal smoking during pregnancy was most common in families with two Finnish parents or an

immigrant father. Having more than two previous births was most common in families with two Finnish parents or two immigrant parents. Low birth weight was least common in families with two Finnish parents. Maternal age, smoking during pregnancy, parity and gestational age were associated with Asperger's syndrome (*p* < 0.1). More detailed descriptions of these associations have been provided previously [23–26].

Table 2 shows the association between parental immigration and the risk of the offspring being diagnosed with Asperger's syndrome. There were 64 children with Asperger's syndrome who had at least one immigrant parent. This equals 3.6 % of all cases, while the corresponding proportion of controls was 5.0 %. There was no significant association between having only an immigrant mother (aOR 1.1, 95 % confidence interval 0.7–1.7) or only an immigrant father (aOR 1.0, 95 % CI 0.7–1.4) and Asperger's syndrome. Having two immigrant parents was associated with a significantly decreased risk of the diagnosis of Asperger's syndrome in the offspring (aOR 0.2, 95 % CI 0.1–0.4). There were no statistically significant differences in the age at diagnosis between the four groups. Among those with Finnish parents, the mean age at diagnosis was 9.7 years (SD 3.3) and the median age was 9 years (range 1–20). Among those with only an immigrant mother, the mean age was 8.4 years (SD 3.0) and the median 8 years (range 5–18). Among those with only an immigrant father, the mean age was 8.4 years (SD 2.7) and the median 8 years (range 2–15). Among those with two immigrant parents, the mean age was 7.7 years (SD 2.0) and the median 7 years (range 6–11).

The regional analysis (Table 3) showed that mothers born in Sub-Saharan Africa had a significantly decreased risk of having a child with Asperger's syndrome (aOR 0.1, 95 % CI 0.01–0.5). The results were similar for fathers born in Sub-Saharan Africa (aOR 0.2, 95 % CI 0.05–0.5). Most Sub-Saharan parents were born in Somalia. Only one child with Asperger's syndrome had a mother born in Somalia while the number of controls with a Somali mother was 65. Similarly, only one child with Asperger's syndrome had a father born in Somalia and the number of controls with a Somali father was 69. No other significant associations

Table 3 Maternal and paternal region of birth by Asperger's syndrome in cases and controls

	Cases		Controls		OR (95 % CI)	<i>p</i>	Adjusted ^a OR (95 % CI)	<i>p</i>
	<i>n</i>	%	<i>n</i>	%				
Mothers								
Finnish	1,752	98.5	6,883	97.0	Ref.			
Western countries	8	0.5	37	0.5	0.9 (0.4–1.8)	0.70	0.9 (0.4–2.0)	0.79
Former Soviet Union and former Yugoslavia	8	0.5	55	0.8	0.6 (0.3–1.2)	0.14	0.6 (0.3–1.3)	0.18
Sub-Saharan Africa	1	0.1	71	1.0	0.1 (0.01–0.4)	0.003	0.1 (0.01–0.5)	0.01
North Africa, Middle East	1	0.1	18	0.3	0.2 (0.03–1.6)	0.14	0.3 (0.03–1.9)	0.19
Asia	8	0.5	35	0.5	0.9 (0.4–1.9)	0.74	0.9 (0.4–2.0)	0.83
Fathers								
Finnish	1,739	97.9	6,836	96.3	Ref.			
Western countries	20	1.1	71	1.0	1.1 (0.7–1.8)	0.67	1.0 (0.6–1.7)	0.94
Former Soviet Union and former Yugoslavia	4	0.2	27	0.4	0.6 (0.2–1.6)	0.28	0.6 (0.2–1.6)	0.27
Sub-Saharan Africa	3	0.1	91	1.3	0.1 (0.04–0.4)	<0.001	0.2 (0.05–0.5)	0.001
North Africa, Middle East	8	0.5	47	0.7	0.7 (0.3–1.4)	0.29	0.7 (0.3–1.4)	0.22
Asia	2	0.1	25	0.4	0.3 (0.1–1.3)	0.11	0.3 (0.1–1.3)	0.10

OR odds ratio, CI confidence interval

^a Adjusted for maternal age, maternal smoking and parity

were shown by the regional analysis, but the direction was the same for other regions as for Sub-Saharan Africa. None of the odds ratios was above 1.0.

An additional analysis including maternal SES was conducted among children for whom this information was available. The four-category variable was used for parental immigration. First, only maternal SES was included in the adjusted analysis. The results remained unchanged. Second, maternal SES was included in the adjusted analysis together with maternal age, maternal smoking and parity. Still no major changes were detected compared with the adjusted analysis conducted without SES. The adjusted odds ratio was 0.2 (95 % CI 0.1–0.5) for two immigrant parents, 1.1 (95 % CI 0.7–1.9) for only an immigrant mother and 1.2 (95 % CI 0.8–1.8) for only an immigrant father.

Discussion

Children born to immigrant parents in Finland have no increased risk of diagnosis with Asperger's syndrome. On the contrary, the risk is significantly decreased among those whose parents are both immigrants. If only one of the parents is an immigrant, the risk does not differ from those with two Finnish parents. The likelihood of being diagnosed with Asperger's syndrome is lowest among children whose parents were born in Sub-Saharan Africa. The results contrast with those in our earlier study which found that children with two immigrant parents had a significantly

increased risk (aOR 1.8, 95 % CI 1.2–2.7) of diagnosis of childhood autism [20]. It also showed an increased risk for children with only an immigrant mother (aOR 1.8, 95 % CI 1.2–2.7), but not for those with only an immigrant father (aOR 1.3, 95 % CI 0.8–1.2). The parental regions of birth with an increased risk were Asia and the former Soviet Union and Yugoslavia. In particular, children of Vietnamese parents had a very high risk (OR 7.0 for maternal and 6.4 for paternal immigration) of being diagnosed with childhood autism. In the current study, none of the cases had a parent born in Vietnam. Two previous studies have also reported that the direction of association between parental migration and childhood autism was opposite to that between parental migration and Asperger's syndrome [13] or Asperger's syndrome together with PDD-NOS [16]. Other previous studies have examined only childhood autism or all ASD subtypes together, which may in part explain the inconsistency in their results.

Opposite directions of association between parental immigration and childhood autism versus Asperger's syndrome may be related to differences in their risk factors. Earlier studies based on the FIPS-A have shown that many obstetric risk factors as well as low birth weight and gestational age are associated with childhood autism, but not with Asperger's syndrome [26, 27]. Also in the FIPS-A, advanced paternal age is associated with childhood autism while advanced maternal age is associated with Asperger's syndrome [25], and second-born children have a higher risk of childhood autism but lower risk of Asperger's syndrome than first-born children [24]. If there are other, unmeasured

factors that are differently associated with the diagnosis of Asperger's syndrome and childhood autism that are also associated with migration, it could explain these findings.

It is possible, however, that the results reflect service use and that not all cases of Asperger's syndrome among children of immigrant parents were included in this register-based study. This is supported by the fact that the risk of Asperger's syndrome was decreased only in children with two immigrant parents. It is reasonable to expect that families with two immigrant parents would face the greatest barriers to service use. It is possible that underdiagnosis is common particularly when the symptoms and functional impairment are not very severe. There was no difference in the age at diagnosis by immigration status, but those with at least one immigrant parent might have more severe symptoms. Children with Asperger's syndrome generally function better in daily life than those with childhood autism and it is possible that their parents do not feel that there is a need to seek help from health services. They may explain their child's behavioral problems in other than medical terms [28] or be reluctant to use mental health services, in particular, because of the risk of becoming stigmatized. Parents who are immigrants may also have less experience navigating the medical system or prefer seeking help through other venues. For example, when the use of mental health service use by Somali adolescents was studied in the USA, it was found that Somali families do not value mental health expertise and that youth more often get help through their friends, school and religious communities [29]. In the Netherlands, children of Turkish or Moroccan origin are referred to mental health institutions specializing in ASD less often than Dutch children [30].

Little is known about the service use of second-generation immigrant children in Finland. A small study conducted in the school health care setting included both first- and second-generation immigrant adolescents and a Finnish comparison group [31]. It found that immigrant students were as healthy as Finnish students, but they were more often reserved when talking with a physician and they and their families had a negative attitude towards a referral to a psychiatric unit. There were also some communication problems, and written information did not reach all parents, because some of them lacked literacy [31]. A register-based study which focused on first-generation adults showed that immigrants use both primary and specialized health services less than those of Finnish origin, though there is variation within the immigrant population by age, sex and region of origin [32]. In two different surveys based on self-reports, Somali respondents have rated their self-experienced health and mental health higher than other immigrant groups or even respondents born in Finland [33, 34]. Interestingly, they reported more visits to a physician than other immigrants or people born in Finland [35], but less

use of mental health services than any of the other groups [34]. A qualitative study showed that Somali immigrants in Finland trust health services when it comes to somatic diseases, but for mental health problems they usually turn to their relatives or consult Muslim healers in Finland or in Somalia [36]. This might explain the strikingly low number of cases with Somali parents in this study.

Even when health professionals assess them, children who have immigrant parents may be less likely to be diagnosed with Asperger's syndrome compared with those whose parents are born in Finland. It has been suggested that even ASD, which certainly has a strong biological etiology, is culturally shaped in symptoms and course [28]. Physicians may have difficulties in understanding the meaning of symptoms if they are not familiar with the cultural context of their patient or if they have communication problems with the patient or his/her parents. Case vignettes were used in a Dutch study, which showed that ASD was less frequently suggested by pediatricians if the patient was not Dutch and they were not explicitly asked to rate the likelihood of ASD [30]. In a US study African-American children received a diagnosis of autistic disorder 1.5 years later than white children even after accounting for entering mental health services at an older age, which means that they required more time in treatment before receiving the diagnosis [37].

Selective migration is another possible hypothesis for the decreased likelihood of being diagnosed with Asperger's syndrome in second-generation immigrants, if parents who themselves have Asperger's syndrome or some of its symptoms are less likely to migrate to a foreign country. This would not, however, explain the increased likelihood of being diagnosed with childhood autism among the children of immigrants to Finland. We do not know if there is more back-migration among families with a child with Asperger's syndrome.

This study has some limitations. The number of immigrants was too small for a more detailed regional analysis. First-generation immigrant children could not be included in the study, since the perinatal data were available for children born in Finland only. No information on the reason of immigration was available. Information on parental SES was limited. The diagnosis of Asperger's syndrome was based on register data and it has not been validated. No information on diagnoses given in specialized outpatient services in public sector was available before year 1998. This information is missing for 2 years, because the ICD-10 codes including the diagnostic code for Asperger's syndrome have been used in Finland since 1996. However, many of the children diagnosed in 1996 or 1997 have probably visited specialized services also later on and are thus included in the register. For private sector, only diagnoses given in the inpatient services were available, but private

inpatient services for children with neuropsychiatric disorders do not exist and the use of private outpatient services is uncommon for this kind of non-acute problems requiring a specialist doctor and usually other professionals as well. Pediatric services in the public sector are free of charge.

Conclusion

This study showed that Finnish children with foreign-born parents are rarely diagnosed with Asperger's syndrome. It is possible that migrant parents might have some protective factors. Alternatively, it may be the underdiagnosis of Asperger's syndrome among second-generation immigrants that explains the results. This issue is worth exploring further, because if these children do not get assessed or they are misdiagnosed, they and their families may miss the support and information they would benefit from, perhaps even more than families with Finnish-born parents. The effect of parental migration should also be taken into account when studying the temporal variation in the incidence of Asperger's syndrome. In addition, this study supports the practice of studying subtypes of ASD separately when examining risk factors. If they are merged into one disorder, important variation in risk factors may remain undetected.

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Conflict of interest The authors declare that they have no conflict of interest.

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