Premigration social adversity: a factor of vulnerability for Autism Spectrum Disorder

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Running Head: Migration and autism

Abstract

Background: Several studies suggest significant relationships between migration and Autism Spectrum Disorder (ASD) but there are discrepant results. Given that no study included a pathological control group, the specificity of the results in ASD can be questioned.

Aims: To compare the migration experience (premigration, migratory trip, postmigration) in ASD and non-ASD pathological control groups, and study relationships between migration and autism severity.

Method: Parents' and grandparents' migrant status was compared in 30 prepubertal ASD boys and 30 prepubertal non-ASD boys with language disorders, using a questionnaire including Human Development Indices (IDH/IDHI) of native countries. Autism severity was assessed using the Child Autism Rating Scale, Autism Diagnostic Observation Schedule and Autism Diagnostic Interview-Revised scales.

Results: The parents' and grandparents' migrant status frequency did not differ between ASD and control groups and was not associated with autism severity. The HDI/IHDI values of native countries were significantly lower for parents and grandparents of ASD children compared to controls, especially for paternal grandparents. Furthermore, HDI/IDHI levels from the paternal line (father and especially paternal grandparents) were significantly negatively correlated with autism severity, particularly for social interaction impairments.

Conclusions: In this study, parents' and/or grandparents' migrant status did not discriminate ASD and pathological control groups and did not contribute either to autism severity. However, the HDI/IHDI results suggest that social adversity-related stress experienced in native countries, especially by paternal grandparents, is potentially a traumatic experience which may play a role in ASD development. A "premigration theory" of autism is then proposed.

Keywords: Autism Spectrum Disorder (ASD); migration; Human Development Index (HDI/HDHI); social adversity; premigration stress.

Autism is a multifactorial disorder involving environmental and genetic factors¹. Some environmental risk factors have been reported for Autism Spectrum Disorder (ASD), such as parental migration.²⁻⁵ Several authors have developed a “migration theory of autism”²⁻⁸ questioning the role of migration among environmental vulnerability factors for autism even if migration has not been associated with any specific mental or psychological conditions.

The updated literature review on migration and autism indicates that studies on this topic are relatively new. Wing⁹ was the first to study potential links between migration and autism. Then, studies compared the frequencies of migrant parents for children with autism and children in the general population, and the frequencies of children with autism in migrant populations and non-migrant populations. Studies were mostly based on the general population registry. The migration experience itself was rarely studied. The main studies on migration and autism are presented in Table 1. They show that paternal migration was not always studied.^{6,11,13,16} Furthermore, Magnusson *et al.*⁷ observed a higher risk of autism when parents have migrated, especially when they came from countries associated with low Human Development Indices (HDI). The HDI is a measure of average achievement in three key dimensions of human development: a long and healthy life, being knowledgeable, and having a decent standard of living.¹⁷ The HDI values vary from 0 (very low HDI) to 1 (very high HDI) and each country is associated with a HDI value. The health dimension is assessed by life expectancy at birth. The education dimension is measured by mean of years of schooling for adults aged 25 years and older and expected years of schooling for children entering school. The standard of living dimension is measured by gross national income (GNI) per capita. There is also the IHDI (Inequality-adjusted Human Development Index) that combines a country’s average achievements in health, education and income with how those achievements are distributed among the country’s population by “discounting” each dimension’s average value according to its level of inequality. HDI/IHDI values of native countries can be used as indicators of premigration

social adversity (the lower HDI/IHDI is, the higher social adversity experience is). Based on the Magnusson study,⁷ it can be hypothesized that lower HDI/IHDI values might be associated with autism.

As shown in Table 1, there are some discrepant results regarding relationships between ASD and migration and no study compared the ASD group to a non-ASD pathological control group. Consequently, it remains unclear whether the association between migration and ASD is specific or not to autism. Given that most environmental risk factors of ASD are also risk factors of other neurodevelopmental disorders, this needs to be investigated.⁵ Also, it remains unclear whether the association between migration and ASD is indirectly related to variables that co-occur often with migration (e.g., trauma, social adversity). The main objective of the present study was to explore the relationships between migration and autism by comparing ASD and non-ASD pathological control groups and studying associations between migration and autism severity. A second objective was to better understand the role of the migration experience (i.e., premigration, migratory trip, or postmigration) as a possible factor of vulnerability for the development of ASD.

+++Insert Table 1 Here+++

Method

Participants

The study was conducted on ASD individuals (N=30) compared to a pathological non-ASD control group (N=30) matched on age, sex and puberty. The two groups did not differ significantly with respect to age, sex and pubertal status. The ASD group included 30 male prepubertal children with autism (mean age: 11.4 years; SD: 2.1 years; range: 7.9-15.7 years) recruited from French day-care

centers. Based on direct clinical observation of the child by two independent child psychiatrists, a diagnosis of autism was made for the ASD group according to the criteria of the American classification (DSM-5)¹⁸, the World Health Organization classification (ICD-10)¹⁹ and the French classification (CFTMEA).²⁰ This diagnosis was confirmed by the Autism Diagnostic Interview-Revised (ADI-R)²¹ and Autism Diagnostic Observation Schedule (ADOS)²² ratings. Indeed, combining information from multiple sources, based on the clinical psychiatric judgment and the administration of the ADI-R completed by the ADOS, is more reliable.²³

The pathological non-ASD control group included 30 male prepubertal children (mean age: 10.7; SD: 2.1 years; range: 8.5-15.5 years) with language disorders who had at least a language examination with a speech therapist in French outpatient care Centers. Based on direct clinical observation of the child by two independent child psychiatrists, a diagnosis of autism was excluded according to the criteria of the DSM-5, ICD-10 and CFTMEA.

Written informed consent was obtained from all parents after explaining the study and its procedure to the parents and their children. The protocol was approved by the ethics committee of the University Hospital of Rennes.

Behavioural and cognitive assessments

The ADI-R is an extensive semi-structured parental interview validated to assess current autistic behavioural impairments and past autistic behavioural impairments that were the most abnormal during the 4 to 5 years-old period. The ADI-R algorithm is based on the 4-to-5year-old period of life. The ADOS is a direct observation of the individual in a standardized semi-structured situation of play. The ADOS Module 1, administered to individuals with no or limited speech, was used in this study. The ADI-R and ADOS were administered by two trained professionals (one child psychiatrist and one psychologist) certified in these scales administration. Also, the Child Autism Rating Scale (CARS)

was used with the ADOS in the same standardized situation of play. The ADI-R, ADOS and CARS scales allowed the assessment of autism severity in major domains of autistic impairments: reciprocal social interaction, communication, repetitive behaviours and stereotyped patterns. In addition, the CARS allowed to get an overall rating of autism severity corresponding to the CARS Total score. The higher the scores are, the more severe are autistic impairments. On the basis of the ADI-R and ADOS algorithms, children with autism (N=30) displayed severe scores of autistic behavioural impairments in repetitive and stereotyped patterns (mean score: 6.20, SD: 2.00 for the ADI-R with a cut-off of 3; mean score: 3.29, SD: 1.24 for the ADOS with no cut-off), reciprocal social interaction (mean score: 25.00, SD: 4.47 for the ADI-R with a cut-off of 10; mean score: 9.43, SD: 2.71 for the ADOS with a cut-off of 7), and communication (mean score: 12.06, SD: 2.43 for the ADI-R non-verbal communication domain with a cut-off of 7; mean score: 5.79, SD: 2.08 for the ADOS communication domain with a cut-off of 4). The mean score (SD) for the Total social communication domain of the ADOS was 15.21 (4.22) with a cut-off of 12. Finally, the CARS-Total mean score (SD) was 40.84 (5.84)(a total score above 30 corresponds to a diagnosis of mild and moderate autism and a total score above 37.5 corresponds to a diagnosis of severe autism).

Furthermore, cognitive functioning was assessed in the ASD group by one psychologist using Raven's Color Progressive Matrices (R-CPM) which is a short (20mn) nonverbal intelligence test validated for young children from 5 years old and individuals with intellectual disability.²⁴ The R-CPM is an instrument of particular interest for intellectual disabled children with ASD.^{25,26} Children with ASD were all cognitively impaired except for three children: sixteen boys were intellectually disabled (Raven class 4 or 5), two boys showed average intellectual functioning (Raven class 3), one boy showed higher intellectual functioning (Raven class 2), and the cognitive assessment was impossible for eleven children in the ASD group (difficulties to understand instructions or too high excitation interfering with the administration).

Migration status assessment

The parents' and grandparents' migration status was assessed using an original questionnaire, developed specifically by the authors, and entitled FEVA (Factors of Environmental Vulnerability to Autism). The FEVA questionnaire was administered during semi-structured parental interviews and included questions on parents and grandparents place of birth allowing HDI/IHDI values associated with native countries to be obtained. Also, based on prior studies the following information was collected: date to family immigration to France (grandparents, parents and/or children), language spoken at home, degree of urbanization in parental living conditions, links with the native country and community, acculturation process, presence of family members in the host country and quality of relationships with these family members, perception of immigration (especially, as a stressful experience), and motivation for leaving native countries.^{6,7,10,13,15,27}

Statistical analyses

The relationships between qualitative variables were analyzed using χ^2 tests or Fisher tests. The comparison of quantitative variables between ASD and control groups was performed using t-tests and analyses of variance (ANOVA). When there was a directional hypothesis (lower HDI/IHDI values might be associated with autism), one-tailed t-test of significance was used. To balance Type I and Type II errors in the statistical analysis of behavioural autistic domains, a hierarchical strategy was used.²⁸ First, the total behavioural domains were examined. If there was a significant result for an overall domain, then a further level of analysis occurred on the sub-scores included in the domain. Correlations between quantitative variables were studied using Bravais-Pearson correlation analyses. Statistical analyses were performed using SAS software.²⁹ The qualitative analysis was conducted

using the grounded theory approach based on categorization and theories concerning cultural, social or psychological phenomenon developed from qualitative empirical data.³⁰

Results

Qualitative results

Migration experience

The reasons to leave native countries were similar for both groups and included fleeing harsh living conditions (reflecting high social adversity), gaining access to graduate studies, employment or high-quality healthcare, and/or joining the partner or other family members already living in France. Both groups reported stress associated with migration when arriving in France concerning administrative problems, memories of hazardous trip, social insecurity and poverty. Also, stress could continue after arriving in France because of administrative problems or family distance when some members were still living in native countries. All migrant families in the ASD and control groups had family members in France before arriving in France (siblings, uncles/aunts, cousins). Good relationships with these family members were reported and parents indicated speaking daily their mother tongue with them. Finally, most of the families for both groups affirmed to prefer staying in France rather than going back to the native country. It is noteworthy that regarding these qualitative data, no differences were found between the ASD and the pathological non-ASD control groups (in the migrant subgroups).

Language spoken at home

In the migrant ASD group, parents declared that they tried to speak exclusively the host country language to their child because they were afraid that the child might get “confused”. However, the

native and host country languages were sometimes used alternately at home with the child in the ASD group. Inversely, migrant parents spoke their mother tongue to the child in the control group.

Relationships between migration and autism

Frequencies of immigrant parents (ASD: n=10/30 families with 7 fathers and 9 mothers; non-ASD: n=5/30 families with 3 fathers and 3 mothers) or immigrant grandparents (ASD: 13/60 families with 8 paternal grandparents and 5 maternal grandparents; non-ASD: 6/60 families with 3 paternal grandparents and 3 maternal grandparents) did not differ significantly between the ASD and the non-ASD control groups, and this result was found regardless of the way in which the migration status was analyzed (at least one parent migrant, only fathers migrant, only mothers migrant, etc.). It is noteworthy that in the control group there was no paternal grandparents who migrated with the father or maternal grandparents who migrated with the mother. Also, for the 9 migrant mothers in the ASD group, two migrations occurred during the perinatal period (one migration three months after delivery and one migration in the third trimester of pregnancy); for the 3 migrant mothers in the control group, no migration occurred during the perinatal period. Except for one child in the ASD group and one child in the control group, all children were born in France. Migrant parents in the ASD group came from the following countries: Algeria, Cameroon, Democratic Republic of Congo, Gabon, Guinea, Haiti, India, Morocco, Sierra Leone and Vietnam. Migrant parents in the control group came from the following countries: Dominican Republic, England, Guinea, Haiti and Turkey.

In the ASD group, no significant relationship was found between parental migration status and autism severity assessed using the ADOS, ADI-R or CARS scales. It is noteworthy that no significant relationship was observed, in particular, between parental migration status and severity of verbal and non-verbal communication impairments assessed on the ADOS, ADI-R as well as CARS scales. Also,

no significant relationship was observed between the language spoken at home to the child (same language as at school or other language) and autism diagnosis when the ASD and control groups were compared or when this comparison focused on the migrant ASD and control subgroups.

Comparison of the migration parental experience in the ASD and control groups

No significant difference was found between the ASD and control groups regarding relationships with the native community (in France or in the native country) and observance of cultural and/or religious rituals, regardless of the way in which the migration status was analyzed (at least one parent migrant, only fathers migrant, only mothers migrant, etc.). Also, no significant differences were observed between the two groups regarding the acculturation experience assessed in our questionnaire (assimilation, rejection of the host country culture, melting pot).

Furthermore, no significant differences were found between the autism and control groups regarding migration-related stress levels when parents arrived in France, but also stress experienced years later related to more long-term consequences of migration such as social isolation.

Finally, no significant relationships were observed between the migration experience (cultural rituals, relationships with the native community, stress levels related to short or long-term immigration effects, etc.) and the severity of autistic behavioural impairments assessed on the CARS, ADOS and ADI-R scales.

Relationships between HDI/IHDI and autism

Mean values of HDI/IHDI were significantly lower for the parents and grandparents in the ASD group, especially for the paternal grandparents, compared to the pathological non-ASD control group (Table 2). It is noteworthy that HDI/IHDI mean values were systematically lower in the ASD group compared to the control group.

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In both groups, migrants had significantly lower HDI/IHDI mean values than non-migrants, showing that migrants come from countries with lower human developmental levels compared to France (in France, HDI=0.897/IHDI=0.813).

Focusing on migrant parents from the ASD and control groups, HDI/IHDI mean values remained systematically lower in the ASD group compared to the control group (it was not possible to test the significance of differences between the two groups due to small samples) and differed between the two groups with regard to human developmental level thresholds: in the migrant ASD group, parents came from countries where human developmental levels were “low” based on IHDI values (or “average” based on HDI values), whereas in the migrant control group, parents came from countries where human developmental levels were “average” based on IHDI values (or “high” based on HDI values).

Finally, HDI and IHDI values from the paternal line (father, paternal grandmother and grandfather) were significantly and negatively correlated with the overall score of autism severity (CARS Total score), especially with the severity of social interaction impairments assessed using the CARS as well as ADOS scales. The lower the HDI/IHDI values were, the more severe current autistic behavioural impairments were, particularly for social interaction impairments (Table 3).

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Discussion

Main finding

The main finding of the study was the absence of significant difference between the ASD and control groups for migration (migratory trip and postmigration experience), whereas HDI/IHDI values of native countries were significantly lower for parents and grandparents in the ASD group compared to the control group and were correlated with autism severity for the paternal line.

Migration and autism

Parents' and/or grandparents' migration did not discriminate the ASD group from the pathological non-ASD control group and was not associated with autism severity. These results are in line with Gillberg *et al.*'s study¹⁶ reporting an absence of significant relationship between parental migration and autism. Given that our two studied groups shared verbal language impairments, potential relationships between migration and language disorders can be questioned. However, no relationship was found in the present study between parental migration and severity of verbal communication impairments in children with autism regardless of the autistic behavioural assessment used (CARS, ADOS or ADI-R). Furthermore, no significant difference was observed between the ASD and control subgroups of migrant parents regarding the language spoken to the child by parents at home (same language as school or other language). This result is in line with those of other studies suggesting no effects of bilingualism on autism development. However, our qualitative results showed that some migrant mothers from the ASD group did not allow themselves to speak their mother tongue with their children (as in the Ijalba study³¹), whereas all migrant mothers from the control group spoke to their children in their mother tongue. These qualitative results suggest that a rupture with children's

mother tongue more than bilingualism might be an environmental factor involved in ASD but these qualitative results were not supported by statistical analyses.

Social adversity and autism

HDI/IHDI values of native countries allow the ASD group to be differentiated from the pathological control group, whereas social adversity levels experienced in the host country (France in our study), measured by parental stress levels when arriving in France and years later, were not significantly different between migrant ASD and control groups and were not associated with autism severity. These results suggest that higher social adversity experienced in native but not host countries is associated with autism (HDI/IHDI values reflect, as previously indicated in the introduction, social adversity levels). The significant association found in the present study between HDI values and autism diagnosis is in line with Magnusson's study.⁷ Interestingly, several studies showing associations between migration and autism concerned native countries with low HDI values, even if HDI values were not specifically reported.^{6,13,16} In addition, relationships between low HDI levels and development of schizophrenia were observed in migrant populations.³² It is noteworthy that, as shown in Table 4, HDI/IHDI values from the paternal line (father, paternal grandmother and grandfather) were significantly and negatively correlated with autism severity (CARS Total score), particularly for social interaction impairments (CARS and ADOS). Furthermore, the strongest correlations were observed for paternal grandparents (the significance was also the highest for them when comparing the HDI/IHDI values in the ASD and control groups; Table 3). Given that half of paternal grandparents migrated without the father (father born in France) in the ASD group, these results suggest, in contrast to Keen *et al.*⁶, that even without parental migration, a risk of developing severe autistic impairments, notably social interaction impairments, exists if paternal grandparents have migrated. How can we understand this ASD risk passed down through paternal line, especially through paternal

grandparents? This transgenerational transmission could come from family history transmission and/or genetic heritage transmission involving epigenetic mechanisms. Indeed, trauma and early life adversity can produce a lasting epigenetic memory which may affect behaviour and mental health status of the next two or three generations.³³⁻³⁵ Interestingly, some authors stated the hypothesis that epigenetic changes in migratory communities might increase ASD risk.⁸ Our study questions epigenetic changes related to social adversity experienced in native countries by parents and/or grandparents. Social adversity may lead to major premigration stress, psychological (perceived stress) as well as biological stress (biological stress responses), independently of potential trauma associated with the migratory trip and postmigration experience; this premigration stress would in turn modify gene expression through epigenetic mechanisms. Epigenetic changes due to social adversity-related stress in native countries could be transmitted to future generations, particularly through the paternal line as suggested by epigenetic studies.^{5,34-37} Furthermore, as indicated in the introduction, migration can be viewed as a “physical act” but also as a “psychic act” passed down to children and involving descendants. Family history in native countries related to premigration social adversity might be transmitted to descendants through the paternal line, especially by paternal grandparents. Social adversity is associated with difficulties to get a social position and take place in the social environment or social group with possible consequences on social interactions. According to several authors,³⁸ social position is most of the time occupied by men compared to women, especially in patriarchal societies (i.e. societies governed/run by men), and socio-economic precarity with its relevant social representation is usually transmitted through the paternal line. It is noteworthy that for the ASD group in the present study, all the mothers’ levels of education were lower or equal to the fathers’ ones, and all the native countries for migrant paternal grand-parents and/or fathers concerned patriarchal societies. Social position has been found to be the only variable, among other social variables such as marital or parental status, with a substantially different effect in male vs. female rates of trauma (low

social position was associated with higher rates of trauma in males than in women).³⁸ This suggests that social adversity experienced in native countries, which involves major difficulty or even impossibility to get a social position and find one's place in the social environment, might be more traumatic for men than women with a risk of transgenerational transmission of this trauma. In line with this idea, autism (a disorder with major social interaction impairments and male prevalence), could be viewed as a social disorder with difficulty to occupy one's place in the social environment. It can be hypothesized that autism might reflect, in migration circumstances, the consequences of social adversity experienced in native countries especially by fathers and paternal grandparents. It is noteworthy that Abraham and Torok³⁹ described the transgenerational transmission of trauma with different steps (first generation: the unspeakable situation, second generation: the unnameable situation, third generation: the unthinkable situation), the third generation expressing the most apparent disorders. This opens new perspectives for potential therapeutic benefits and prevention of ASD in migrant families (at least for decreasing social interaction impairments) by working on verbal expression, narration and representation of social adversity-related stress experienced in native countries, especially by the paternal line.

Importance of the premigration experience

Concerning the association between autism and migration reported by prior studies, it may not be migration but rather coming from countries with low HDI/IHDI that could be a factor of vulnerability for autism. Therefore, the risk for autism would be more related to social adversity experienced in native countries by parents and grandparents before migration (reflected by HDI/IHDI values) than migration itself. Our results highlight the importance of the premigration experience. Migration needs

to be integrated in the framework of a trajectory which cannot be limited to the migratory trip and the postmigration experience but includes also the premigration experience. This trajectory results in biological responses (including genetic expression) and psychological responses. As some authors have developed the “migration theory of autism”⁸, we propose the “premigration theory of autism” stating that social adversity-related stress experienced in native countries might be associated with autism.

Study limitations

Some limitations of the current study should be acknowledged. Sample sizes were small and the study is therefore exploratory. Furthermore, in the present study only two families migrated during the perinatal period. Given that higher migration-related stress vulnerability was observed during the perinatal period (more precisely, during the year before the child’s birth according to Magnusson *et al.*⁷), effects of the migratory trip and early post-migratory experience on the development of ASD might be underestimated in this study.

Implications

In conclusion, the findings show that premigration social adversity but not migration (migratory trip and postmigration experience) is significantly associated with autism. This is, to our knowledge, the first study on migration in autism to compare ASD and pathological non-ASD control groups in order to test the specificity of the results in autism. However, we cannot rule out possible effects of migration-related stress when the migration experience occurs during pregnancy. Furthermore, our results suggest that premigration-related stress, such as social adversity in native countries experienced by parents and grandparents (especially paternal grandparents) reflected by low HDI/IHDI values, might play a role in the development of ASD for the descendants. The findings underline the importance of considering HDI/IHDI values of native countries, especially paternal

grandparents' ones, when studying relationships between migration and autism in future research. Finally, a premigration theory of autism can be proposed stating that social adversity-related stress experienced in native countries might be a traumatic experience and factor of vulnerability for Autism Spectrum Disorder. Premigration stress effects would be transmitted over several generations through paternal lineage (particularly by paternal grandparents) with genetic heritage (involving epigenetic mechanisms) and/or family heritage (involving narration and filiation).

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Author Contribution: ST conceived and designed the study. NA, SL and IL conceived and designed the migrant status questionnaire, and NA administered this questionnaire during semi-structured parental interviews for all participants. ST, JX, DC, SK, LG, VM, ACR, and MBou, recruited the children of the ASD group, and NA and IL recruited the children of the control group. SK, JX, and VM participated to the behavioral assessments of autism severity. ST and NA performed the data analysis. NA and ST wrote the manuscript, and all authors commented on the manuscript and revised the article.

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Table 1 Studies on migration and autism.

Study	Population	Sample size	Main results
Gillberg, 1987 ¹⁰	Epidemiological study based on a Swedish population registry comparing migrant parents' frequency between autism and control group	35 children with autism, 20 living in urban area and 15 living in rural area for 42886 children in general population from same region, matched on age	30% urban children with autism have migrant parents; 0% rural children with autism have migrant parents; non-significant difference regarding migrant parents' frequency between urban ASD and typically developing control groups; significantly lower migrant parents' frequency between ASD rural and typically developing control groups (p <0.001)
Gillberg, 1995 ¹¹	Study of autism prevalence in children born in Sweden from mothers born in Uganda	3 children with autism born in Sweden from mothers born in Uganda	Autism prevalence in children born in Sweden from mothers born in Uganda (15%) compared to prevalence of autism in general population (0.08%)
Gillberg et al., 1996 ¹²	Epidemiological study based on a Swedish population registry comparing migrant parents' frequency between an autism and a control group	55 children with autism for 78106 children in general population	27% children with autism compared to 26.2% children in general population have migrant parents (non-significant)
Lauritsen et al., 2005 ¹³	Epidemiological study based on a Danish population registry comparing migrant parents' frequency between an autism and a control group	818 children with autism born in Denmark from a cohort of 943 664 children in general population	Relative risk of ASD evaluated at 1.42 when mothers born outside European continent compared to mother born in Denmark.
Keen et al., 2010 ⁶	Retrospective study based on English population registry comparing ASD prevalence according to mother's native country and her ethnic group	428 children with autism	Relative risk of autism higher for children whose mothers born in the Caribbean (OR = 10.01, CI 95% 5.53-18.1), in Asia (OR = 3.97, CI 95% 2.01-7.84), in Africa (OR = 7.92, CI 95% 5.39-11.6)
Barnevik-Olsson et al., 2010 ¹⁴	Epidemiological study based on a Swedish population registry focusing on autism prevalence in Somali background population compared to non-Somali population	-250 children with autism (232 non-Somali et 18 Somali) -113391 children in general population (111555 non-Somali and 1836 Somali)	Autism prevalence higher in Somali background children compared to non-Somali children (p<0.001)
Magnusson et al., 2012 ⁷	Case-control study based on population registry (Stockholm youth cohort) comparing migrant parents' frequency between an autism and a control group	3918 children with autism (2269 high functioning and 1649 low functioning) for 589 114 children in general population	Relative risk of low functioning autism higher in migrant population when the two parents were migrant (OR = 1.5, CI 95%: 1.3-1.7), mainly if parents came from country associated with low Human Development Index
Schieve et al., 2012 ¹⁵	Study based on an American population registry comparing ASD prevalence according to ethnic origin (Hispanic) and parents' native country; control group (children whose parents born in USA and non-Hispanic)	Control group consisting of 34996 children	Significantly higher ASD prevalence (1.19%) in the control group compared to Hispanic children born in USA whose both parents were born abroad (0.31%)
Becerra et al., 2014 ¹⁶	Epidemiological study based on an American population registry comparing autism prevalence according to mother's native country and ethnicity	7540 children with autism from a cohort of 1 626 354 children in general population matched on age	Higher relative risk of autism when mothers are Asian and born in Philippines (OR = 1.23, CI: 1.08-1.40) or in Vietnam (OR = 1.45, CI: 1.24-1.70) compared to white mothers born in USA

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Table 2 Comparison of mean values (SD) of Human Development Index (HDI) and Inequality-adjusted Human Development Index (IHDI) of native countries between Autism Spectrum Disorder (ASD) and control groups.

HDI/ IHDI		ASD (N = 30)	Control (N = 30)	DF	<i>t</i> value	<i>P</i> value
HDI	Mother	0.82 (0.14)	0.86 (0.09)	58	1.69	0.045
	Father	0.83 (0.14)	0.88 (0.07)	40.8	1.71	0.045
	MGM	0.82 (0.14)	0.87 (0.09)	58	1.63	0.050
	MGF	0.81 (0.14)	0.87 (0.09)	51.1	1.90	0.030
	PGM	0.81 (0.15)	0.87 (0.07)	41	2.08	0.020
	PGF	0.81 (0.15)	0.87 (0.07)	40.6	2.11	0.020
IHDI	Mother	0.71 (0.17)	0.78 (0.12)	58	1.67	0.050
	Father	0.73 (0.17)	0.79 (0.09)	42.8	1.65	0.050
	MGM	0.71 (0.17)	0.77 (0.12)	58	1.62	0.055
	MGF	0.70 (0.17)	0.77 (0.12)	58	1.90	0.030
	PGM	0.71 (0.18)	0.78 (0.09)	42.7	2.01	0.025
	PGF	0.70 (0.18)	0.78 (0.09)	42.6	2.20	0.015

Note: DF, degree of freedom; MGM, maternal grandmother; MGF, maternal grandfather; PGM, paternal grandmother; PGF, paternal grandfather.

Table 3 Bravais-Pearson correlations in children with Autism Spectrum Disorder (N=30) between HDI/IHDI values of native countries and autism severity scores (only domains with significant results are presented with Pearson *r* and *P* values).

Scales	CARS Total	CARS Social Interaction	ADOS Social Interaction	ADOS Play
HDI/IHDI				
Father				
HDI	<i>r</i> = -0.40 <i>P</i> = 0.03	<i>r</i> = -0.36 <i>P</i> = 0.05	<i>r</i> = -0.33 <i>P</i> = 0.08	<i>r</i> = -0.31 <i>P</i> = 0.10
IHDI	<i>r</i> = -0.41 <i>P</i> = 0.03	<i>r</i> = -0.37 <i>P</i> = 0.05	<i>r</i> = -0.32 <i>P</i> = 0.09	<i>r</i> = -0.32 <i>P</i> = 0.10
Paternal Grandmother				
HDI	<i>r</i> = -0.46 <i>P</i> = 0.01	<i>r</i> = -0.48 <i>P</i> = 0.01	<i>r</i> = -0.41 <i>P</i> = 0.03	<i>r</i> = -0.38 <i>P</i> = 0.04
IHDI	<i>r</i> = -0.46 <i>P</i> = 0.01	<i>r</i> = -0.49 <i>P</i> = 0.008	<i>r</i> = -0.41 <i>P</i> = 0.03	<i>r</i> = -0.39 <i>P</i> = 0.04
Paternal Grandfather				
HDI	<i>r</i> = -0.46 <i>P</i> = 0.01	<i>r</i> = -0.48 <i>P</i> = 0.009	<i>r</i> = -0.42 <i>P</i> = 0.03	<i>r</i> = -0.38 <i>P</i> = 0.04
IHDI	<i>r</i> = -0.41 <i>P</i> = 0.03	<i>r</i> = -0.44 <i>P</i> = 0.02	<i>r</i> = -0.36 <i>P</i> = 0.04	<i>r</i> = -0.42 <i>P</i> = 0.03

Note: HDI, Human Development Index; IHDI, Inequality-adjusted Human Development Index; CARS, Child Autism Rating Scale; ADOS, Autism Diagnostic Observation Schedule.