## Maternal Immigrant Status and Signs of Neurodevelopmental Problems in Early Childhood: The French Representative ELFE Birth Cohort

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A growing body of evidence suggests that children of immigrants may have increased risks of neurodevelopmental disorders. However, evidence based on parent report and on very young children is lacking. We therefore investigated the association between maternal immigrant status and early signs of neurodevelopmental problems in a population-based sample of 2-year-old children using standardized parent-report instruments. We used data from the French representative Étude Longitudinale Française depuis l'Enfance birth cohort, initiated in 2011. The study sample included 9,900 children of nonimmigrant French, 1,403 children of second, and 1,171 children of first generation immigrant women followed-up to age 2 years. Neurodevelopment was assessed using the Modified Checklist for Autism in Toddlers (M-CHAT) and an adaptation of the MacArthur-Bates Communicative Development Inventories (MB-CDI). In fully adjusted linear regression models, maternal immigrant status was associated with M-CHAT scores, with stronger associations in children of first ( $\beta$ -coefficient: 0.19; 95% CI 0.08–0.29) than second generation immigrants (0.09; 0.01–0.17). This association was especially strong among children of first generation immigrant mothers native of North Africa (vs. nonimmigrant French: 0.33; 0.16–0.49) and French-speaking Sub-Saharan Africa (0.26; 0.07–0.45). MB-CDI scores were lowest among children of first generation immigrant mothers, particularly from mostly non-francophone regions. Children of first generation immigrant mothers were most likely to have simultaneously low MB-CDI and high M-CHAT scores. Our findings suggest that maternal immigrant status is associated with early signs of neurodevelopmental difficulties, with strong variations according to maternal region of origin. Further research is necessary to test whether these associations persist and to determine the underlying mechanisms. Autism Res 2019, 12: 1845-1859. © 2019 International Society for Autism Research, Wiley Periodicals, Inc.

Lay Summary: We asked immigrant and nonimmigrant mothers in France about early signs of neurodevelopmental problems in their 2-year-old children. Overall, we found that children of immigrants may be at higher risk of showing these early warning signs, as compared to children of nonimmigrants. This is in line with previous studies, which were based on doctors' diagnoses at later ages. However, our results differed depending on the mothers' regions of origin. We found the highest risks in children of first generation immigrants from North and French-speaking Sub-Saharan Africa, who also seemed especially at risk of neurodevelopmental problems combined with low language development.

Keywords: developmental disabilities; autism spectrum disorder; language; child development; immigrants

#### Introduction

Neurodevelopmental disorders are a heterogeneous group of conditions originating from nontypical development of the central nervous system, which result in difficulties in communication, motor, and social skills, as well as learning, memory, and cognition [Abdullahi et al., 2018]. Neurodevelopmental problems in children represent a

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**Data Availability Statement:** The data that support the findings of this study are available from the ELFE team (https://www.elfe-france.fr/). Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of the ELFE team.

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significant public health burden in France [Delobel-Ayoub et al., 2015], similarly to other industrialized countries, such as United States [Boyle et al., 2011]. Approximately 0.36% of French children are estimated to have autism spectrum disorder (ASD), 0.18% with and 0.16% without comorbid intellectual disability [Delobel-Ayoub et al., 2015], and 0.18% are estimated to have severe intellectual disabilities without ASD [Delobel-Ayoub et al., 2015]. Signs of many neurodevelopmental disorders, such as ASD, may already be present in early childhood, long before diagnoses are typically made [Chlebowski, Robins, Barton, & Fein, 2013]. A growing body of literature recognizes that interventions during this time period can be highly beneficial, which is why increasing efforts have been made to study these early warning signs, which may include problems in motor skills (no climbing, unusual finger movements, no walking, dropping toys), social interactions (no mirroring parents' smile, no eye contact, no interest in other children), early theory of mind/joint attention (no pointing to express interest, no showing objects), language and communication (no expression of own wishes, no understanding "no," no pointing to request), as well as sensory abnormalities [under- or over-sensitivity to noise; Robins, Fein, Barton, & Green, 2001].

Mounting evidence suggests that children of immigrant and ethnic minority parents are at increased risk of various neurodevelopmental problems, such as Attention Deficit and Hyperactivity Disorder [ADHD; Lehti, Chudal, Suominen, Gissler, & Sourander, 2016], impaired language development [Lehti, Gyllenberg, Suominen, & Sourander, 2018], intellectual disability [Abdullahi et al., 2018, 2019], and ASD [Abdullahi et al., 2018, 2019; Crafa & Warfa, 2015; Dealberto, 2011; Kawa et al., 2017]. While the strength of the association between parental immigrant status and offspring neurodevelopmental problems, including ASD, varies across studies, systematic reviews have found support for this association [Abdullahi et al., 2018; Crafa & Warfa, 2015; Dealberto, 2011; Kawa et al., 2017; Ng, de Montigny, Ofner, & Docé, 2017]. There is suggestion that elevations in ASD risk in children of immigrants are mainly attributable to particular neurodevelopmental phenotypes, characterized by intellectual disability and language delay [Abdullahi et al., 2019; Dealberto, 2013]. Children of first generation immigrants may be at higher risk than those of second generation immigrants or nonimmigrant ethnic minority parents, but evidence in this area is mixed and results vary depending on the mother's region of origin. In the United States, Becerra et al. [2014] found that children of women born in the Philippines and Vietnam have higher risks of ASD as compared to children of USborn White mothers, while children of women born in China, Japan, or Korea, or Asian women born in the United States do not have an elevated risk. Among Hispanic mothers, only those born in Central/South America or in the United States have higher risks of having a child with ASD, while no association was found in children of mothers born in Mexico. Both children of United States- and foreign-born Black mothers have significantly higher risks of ASD, especially children of Black mothers born abroad. The importance of the experience of migration itself is further highlighted by evidence suggesting a higher incidence of low-functioning autism in children whose mothers migrated during the year before giving birth [Magnusson et al., 2012].

Risk factors most consistently associated with neurodevelopmental problems, such as ASD, are prenatal and include male sex [Loomes, Hull, & Mandy, 2017], advanced parental age [Guinchat et al., 2012; Huang, Zhu, Qu, & Mu, 2016], premature birth [Guinchat et al., 2012; Huang et al., 2016], low birth weight [Guinchat et al., 2012; Huang et al., 2016], birth order [Guinchat et al., 2012; Huang et al., 2016], delivery by caesarean section [Guinchat et al., 2012], and pregnancy complications, such as breech presentation [Guinchat et al., 2012], gestational diabetes [Guinchat et al., 2012; Huang et al., 2016], blood loss [Guinchat et al., 2012], and preeclampsia [Guinchat et al., 2012; Huang et al., 2016]. Further risk factors include maternal obesity [Sanchez et al., 2018], smoking [Wehby, Prater, McCarthy, Castilla, & Murray, 2011], alcohol use [Landgren, Svensson, Stromland, & Andersson Gronlund, 2010], certain medications [Ng et al., 2017], infections [Al-Haddad et al., 2019], and exposure to toxic substances [Ng et al., 2017]. Maternal stress and poor mental health in pregnancy are also suspected to be related to neurodevelopment, but the level of evidence is less conclusive [Ibanez et al., 2015; van den Bergh et al., 2017]. Prenatal and perinatal risk factors may affect the developing brain directly [e.g., white matter injury related to prematurity; Movsas et al., 2013] or indirectly. For example, adverse conditions in utero and during delivery may lead to changes in epigenetic profiles, gene expression, as well as neurotransmitters and proteins important for central nervous system development [van den Bergh et al., 2017; Wadhwa, Buss, Entringer, & Swanson, 2009]. Furthermore, early childhood exposures, such as childcare arrangements [Gomajee et al., 2018], (lack of) child stimulation [Gomajee et al., 2018; Rutter, 1998], (multiple) language exposure [Uljarević, Katsos, Hudry, & Gibson, 2016; Lehti et al., 2018], and screen use time [Christakis, Ramirez, Ferguson, Ravinder, & Ramirez, 2018; Wu et al., 2017] may also play a role in variations in early child development, but have been studied less frequently and are less clearly linked to clinical disorders. It must therefore be noted that delays in development related to such early childhood factors might not be permanent and indicative of a lifelong condition, such as ASD [Rutter, 1998] but rather transient and amenable to change.

Many pre-, peri-, and post-natal factors associated with children's neurodevelopment may vary with parental immigrant status. For example, both second and first generation immigrant women can face cultural and language barriers in accessing prenatal care, resulting in deferred treatment of pregnancy complications [Heaman et al., 2013]. Furthermore, on average immigrants differ from the host population in terms of obesity [Martin-Fernandez, Grillo, Tichit, Parizot, & Chauvin, 2012], socioeconomic status, as well as associated risk factors such as poor housing [Delobel-Ayoub et al., 2015; Douzet & Robine, 2015; Racape, Schoenborn, Sow, Alexander, & De Spiegelaere, 2016]. Immigrants are at risk of discrimination, which may affect mental health [Ikram et al., 2015] and impair access to vital everyday life services [Heaman et al., 2013; Vignier, Spira, Bouchaud, du Loû, & Chauvin, 2018]. Exposure to such stressors might also adversely influence health behaviors [Visser, Ikram, Derks, Snijder, & Kunst, 2017] and physical health [Ikram et al., 2017], which subsequently may impact the health of the fetus [Huang et al., 2016; Sanchez et al., 2018]. Additionally, first generation immigrants from certain world regions may have faced severe stressors prior to or during migration, such as armed conflict, sexual violence, or extreme deprivation [Kalt, Hossain, Kiss, & Zimmerman, 2013]. Such experiences may have a lasting impact on stress physiology [e.g., hypothalamic-pituitary-adrenal axis dysregulation; Klaassens et al., 2009] and mental health [Kalt et al., 2013], which in turn could adversely affect fetal neurodevelopment [van den Bergh et al., 2017]. Second generation immigrants may face other types of stressors, such as those related to labor market discrimination and neighborhood segregation [Douzet & Robine, 2015]. Finally, postnatal factors, such as child stimulation, childcare arrangements, screen use time, and multiple language exposure might differ depending on parental immigrant status. Additionally, many risk factors associated with children's developmental problems may vary according to parents' ethnicity as well as the circumstances of migration [Gerritsen et al., 2006; Ikram, Kunst, Lamkaddem, & Stronks, 2014].

There are several gaps in the existing literature on the relationship between maternal immigrant status and offspring neurodevelopmental problems. We were unable to identify any studies that assessed the association between parental immigrant status and neurodevelopmental problems in nonclinical settings, as existing research exclusively focused on children with diagnosed neurodevelopmental disorders, such as ASD. These studies are not exhaustive as they miss very young children who are not yet diagnosed, those who remain undiagnosed, and those with subclinical or less severe symptoms [Magnusson et al., 2012]. Studying immigrants' children in nonclinical samples is particularly important as there is evidence of ethnic diagnostic/referral bias in medical practice [Begeer, Bouk, Boussaid, Terwogt, &

Koot, 2009]. The associated risk of late diagnosis and underdiagnosis [Kawa et al., 2017] might lead to a higher likelihood of missing problems in immigrants' children when using routine clinical data, and hence result in underestimates of neurodevelopmental inequalities in the population. Furthermore, most children diagnosed with neurodevelopmental conditions, such as ASD, first receive a diagnosis when aged 3 years or older, although signs may be present earlier [Chlebowski et al., 2013]. Therefore, currently very little is known about the neurodevelopmental health of immigrants' children at young ages, even though interventions during those early developmental periods seem particularly beneficial [Chlebowski et al., 2013]. Importantly, existing research based on clinical diagnoses does not capture the natural variation in early development in the population and lacks information on temporary delays in very young children that do not necessarily lead to the diagnosis of a lifelong condition. Further limitations pertain to the design of existing studies, which are mainly based on disease registers or retrospective case-control studies. Retrospective information collected from families might be influenced by information and recall bias [Abdullahi et al., 2018; Crafa & Warfa, 2015; Dealberto, 2011; Kawa et al., 2017]. Studies based on registers, particularly in Scandinavian countries, circumvent this type of bias, but are frequently less comprehensive in measuring individuals' characteristics, including patterns of children's neuro- and lexical development, and may lack important covariates, such as maternal mental health symptoms or the child's multiple language exposure. Particularly, the lack of information on children's language exposure is an important omission as a seemingly higher incidence of ASD with comorbid language delay could be related to differences in skill acquisition (e.g., as a result of multiple language exposure or insufficient parental knowledge of the host country's language) rather than true differences between children of immigrants and nonimmigrants [Lehti et al., 2018]. Differences in language development are not uncommon in bilingual children, as language acquisition may not progress at the same speed in both languages [Lehti et al., 2018]. To our knowledge, there is currently no evidence from prospective cohort studies investigating early signs of neurodevelopmental problems according to parental immigrant status using standardized parent-report instruments in population-based samples.

#### Aims of the Study

We aimed to identify relations between maternal immigrant status and offspring neurodevelopmental problems at 2 years. We further aimed to identify variations by maternal region of origin and assess the role of pre-, peri-, and selected postnatal risk factors in this association.

### Material and Methods

Study Population

"Étude Longitudinale Française depuis l'Enfance" (ELFE) is a nationally representative birth cohort of N = 18,329 children born in France in 2011. A detailed description of the cohort can be obtained elsewhere [Vandentorren et al., 2009]. The study interviews were conducted either face-to-face or by telephone and could be completed in French, English, Arabic, Turkish, Bambara, Soninke, and Wolof.

#### Immigrant Status

To capture the impact of migration across generations, mothers were classified based on their own and their parents' citizenship as nonimmigrant French (born to two parents who had French citizenship at birth), second generation immigrant (French citizenship at birth and at least one non-French or naturalized parent), and first generation immigrant (either non-French or naturalized). All immigrant women were further classified based on their own or their parents' birth region as follows: European Union (EU), North Africa, French-speaking Sub-Saharan Africa, or "other" region. These regions are those with the highest migration to France [Bouvier, 2012]. Moreover, we distinguished women originating (themselves or their parents) from mostly francophone regions (North Africa [Morocco, Tunisia, and Algeria], French-speaking Sub-Saharan Africa) from those who were from mostly nonfrancophone regions (EU, "other" regions). Second generation immigrant women were classified according to the birth region of their non-French/naturalized parent(s). If parents came from different regions, precedence was given to the mother's birth region. First generation immigrants were classified according to their own birth region if born outside of France. In the rare case that a woman we classified as first generation immigrant was born in France, she was grouped according to the birth region of her parents, as described above. Information regarding the mother's birth region and her citizenship was obtained by self-report at the time of the child's birth. Information regarding the grandparents' birth region and their citizenship was obtained from each parent at 2 months.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The ELFE study received approval from France's consultative committee for the treatment for health information for research (CCTIRS) and the national data protection authority (CNIL). Written informed consent was obtained from all participants prior to inclusion in the study.

#### Study Outcomes—Neurodevelopmental Problems at 2 Years

Modified checklist for autism in toddlers (M-CHAT). Children's general neurodevelopment at age 2 years was assessed using the Modified Checklist for Autism in Toddlers (M-CHAT) questionnaire, a validated screening instrument for neurodevelopmental problems in children aged 16-30 months, including early signs of ASD [Baduel et al., 2017; Chlebowski et al., 2013]. The M-CHAT questionnaire consists of 23 yes/no items [Chlebowski et al., 2013]. We used both the recommended cut offs [low risk = 0-2; intermediate risk = 3-6; high risk = 7-23; Chlebowski et al., 2013] and the overall score, ranging from 0 to 23, which may be a closer representation of natural variations in neurodevelopment in the population. A detailed description of the cut offs, including test performance indicators for ASD, "any DSM-IV diagnosis," and "any DSM-IV diagnosis + developmental concerns" can be found elsewhere [Chlebowski et al., 2013].

MacArthur-Bates development communicative inventories—words and sentences—short form (MB-CDI). Children's language skills at 2 years were assessed with an adapted short version of the MacArthur-Bates communicative development inventories-words and sentences scale [MB-CDI; Kern, Langue, Zesiger, & Bovet, 2010]. Mothers were asked if their child spontaneously produced 100 predefined words considered indicative of lexical development at 24 months. The MB-CDI was studied as a continuous score (range 0-100). The French version of this instrument was validated by Kern et al. [2010] and has shown good reliability. We used the lowest decile (i.e., expressive use of no more than 32 of the predefined words) as indicator of low lexical development. The MB-CDI was completed in the interview language requested by the mother.

#### Covariates

Covariates, including risk factors of children's neurodevelopmental disorders, were selected based on systematic reviews [Gardener, Spiegelman, & Buka, 2011; Guinchat et al., 2012; Huang et al., 2016; Ng & de Montigny, 2017].

- 1. *Demographic characteristics* reported by the mother at the time of the child's birth include maternal age, paternal age, recruitment wave, and residential area.
- 2. *Socioeconomic characteristics* reported by the mother at the time of the child's birth include maternal educational attainment, maternal employment in pregnancy, and paternal employment.
- 3. *Maternal health characteristics* reported by the mother at the time of the child's birth include daily smoking

and alcohol use during pregnancy, as well as Body Mass Index prior to pregnancy.

- 4. *Pregnancy and child characteristics* collected from the child's medical record include child sex, parity, twin birth, number of prenatal visits, caesarean section, gestational age, birth weight, and selected pregnancy complications.
- 5. *Psychosocial characteristics* reported by the mother at the time of the child's birth include persistent mental health problems during pregnancy, subjective mental distress, and spousal support.
- 6. *Postnatal characteristics* reported by the mother when the child was 1 year include childcare arrangements at 1 year and screen use time at 1 year.
- 7. *Child exposure to multiple languages* was assessed by parental report both 1 and 2 years after birth.

#### Statistical Analysis

To test associations between maternal immigrant status and children's neurodevelopment, we first modeled both outcomes as continuous measures using linear regression. Changes in estimates after sequentially adjusting for different groups of covariates are presented in Table S1. Second, we studied the recommended M-CHAT cut offs with unordered multinomial logistic regression and the odds of belonging to the first decile on the MB-CDI with logistic regression. Third, we conducted stratified analyses to assess whether the association between maternal immigrant status and the M-CHAT varied with children's level of lexical development assessed with the MB-CDI. Overall, the amount of missing information among women who participated in the survey at 2 years was small, with the highest proportions of observations missing for childcare arrangements (4.9%), screen use time (3.7%), and paternal age (3.5%). Missing data on all covariates were imputed using multiple imputations by chained equations under fully conditional specification under the assumption of missingness at random [van Buuren, 2007]. Ten imputed data sets were created using a generalized logit distribution with 100 iterations between data sets. All analyses were conducted using SAS 9.4 (SAS/STAT 14.2).

#### Results

Of the 18,329 children initially enrolled in ELFE, N = 13,342 were reassessed at age 2 years via maternal reports. We excluded children with incomplete maternal reports on the M-CHAT (N = 517) or MB-CDI (N = 511), as well as children with auditory problems (N = 108). There is evidence of unequal dropout by immigrant status in ELFE. While at baseline (Table S2), 12.14% of children had a second and 13.25% a first generation immigrant mother, our study sample only included 11.25% children of second

and 9.39% children of first generation immigrant mothers. Furthermore, women included in our sample were slightly older, had higher educational attainment, and were more likely to have been employed during pregnancy. Table 1 presents characteristics of the study population by maternal immigrant status. Our sample included N = 9,900 children of nonimmigrant French, N = 1,403 of second, and N = 1,171 of first generation immigrant mothers. Information on maternal immigrant status was missing for N = 245 children in the study sample.

We observed a gradient (one-way analysis of variance [ANOVA], F = 44.79, P < 0.001) in mean M-CHAT scores across immigrant groups (average scores respectively 1.48, 1.64, and 1.87 in children of nonimmigrant French, second, and first generation women). Likewise, as compared to nonimmigrant French mothers (0.53%), a higher proportion of children of second generation (0.86%) and first generation immigrants (0.77%) were in the M-CHAT "high risk" category. Similarly, we found a gradient regarding "intermediate risk," with 18.15% of children of nonimmigrant French women in this group, as compared to 21.81% of children of second generation and 28.86% of children of first generation immigrants. These differences were statistically significant ( $\chi^2 = 85.49$ , P < 0.001). Differences in mean MB-CDI scores were statistically significant (one-way ANOVA, F = 6.92, P = 0.001), with slightly lower scores in children of first generation immigrants. However, no statistically significant differences ( $\chi^2 = 1.77$ , P = 0.413) were found when considering the proportion of children scoring in the lowest decile of the MB-CDI. The lowest reported M-CHAT score was 0 and the highest was 19. The range of reported MB-CDI scores was 0-100.

In bivariate linear regression analyses (Table 2), maternal immigrant status was significantly associated with children's M-CHAT scores, with stronger associations in children of first generation mothers. These associations were attenuated but remained statistically significant after adjustment for covariates. Adjustment for socioeconomic status, childcare arrangements, and screen use time led to the greatest changes in coefficients. Associations remained largely unaffected when taking into account demographic characteristics, maternal health, psychosocial characteristics, pregnancy and child characteristics, and multiple language exposure (Table S1).

Furthermore, we found variations depending on the mother's region of origin, with significant bivariate associations in all groups except for children of women originating from the EU. After controlling for covariates, only children of first generation immigrants from North or French-speaking Sub-Saharan Africa as well as children of second generation immigrants from "other" regions had significantly elevated scores. Regarding the MB-CDI, in bivariate analyses (Table 2), compared to children of nonimmigrant women, only children of first generation immigrants, particularly those from "other" regions, had lower

	Nonimmigrant French		Second generation immigrant		First generation immigrant	
	N	(%)	N	(%)	N	(%)
Immigrant status	9,900	(79.37)	1,403	(11.25)	1,171	(9.39)
Region of origin						
Nonimmigrant French	9,900	(100)	-	-	-	-
EU (excl. France)	-	-	588	(41.91)	227	(19.39)
North Africa	-	-	454	(32.36)	351	(29.97)
French-speaking Sub-Saharan Africa	-	-	110	(7.84)	250	(21.35)
"Other" regions	-	-	251	(17.89)	343	(29.29)
1. Demographic characteristics				, ,		
Maternal age $\geq$ 30 years	6,074	(61.57)	866	(61.81)	766	(66.03)
Advanced paternal age (>40 years)	1.173	(12.19)	173	(12.81)	336	(31.20)
Recruitment wave	,					
April	1.473	(14.88)	207	(14.75)	179	(15.29)
June_July	2 566	(25.92)	336	(23.95)	300	(25.62)
Sentember-October	2 822	(28.51)	418	(29.79)	330	(28.18)
November-December	3 039	(30.70)	442	(31 50)	362	(30.91)
Residential area	5,055	(30.70)		(51.50)	302	(30.31)
Île-de-France	1 533	(15.49)	446	(31 70)	493	(42 14)
Paris Basin	1,555	(18.85)	160	(11 40)	136	(11.62)
North Pas de Calais	027	(10.05)	100	(11.40)	57	(11.02)
Norui-Fas de Calais	057	(0.40)	90	(0.04)	57	(4.07)
EdSL	905	(9.75)	141	(10.05)	95	(6.12)
West	1,004	(17.01)	70	(5.50)	01 70	(0.92)
South-West	831	(8.40)	110	(7.84)	79	(0.75)
Centre-Edst	1,183	(11.95)	1/5	(12.47)	83	(7.09)
South	1,001	(10.11)	197	(14.04)	140	(12.48)
2. Socioeconomic characteristics						
Maternal education		(44.70)	005	(4 ( 60)	o ( o	(00.67)
1 (lowest)	1,161	(11./3)	206	(14.68)	242	(20.67)
2 (intermediate)	1,687	(17.04)	269	(19.17)	241	(20.58)
3 (highest)	7,052	(/1.23)	928	(66.14)	688	(58.75)
Mother unemployed/ not in the labor force (in pregnancy)	1,293	(13.27)	258	(18.74)	435	(39.47)
Father unemployed/ not in the labor force	459	(4.73)	100	(7.28)	153	(13.72)
3. Maternal health						
Smoking	1,826	(18.61)	236	(16.97)	89	(7.77)
Alcohol consumption	2,694	(27.47)	261	(18.76)	222	(19.44)
Body Mass Index ≥25	2,507	(25.64)	392	(28.30)	359	(31.46)
4. Pregnancy & child characteristics						
Male sex	5,001	(50.94)	671	(48.31)	586	(50.65)
Multiparity	5,310	(53.64)	753	(53.67)	668	(57.05)
Twin birth	306	(3.11)	48	(3.45)	41	(3.53)
Number of prenatal visits						
<7	811	(8.31)	119	(8.69)	130	(11.73)
7–8	4,637	(47.51)	629	(45.91)	485	(43.77)
>9	4,312	(44.18)	622	(45.40)	493	(44.49)
Caesarean section	1,698	(17.60)	288	(21.02)	276	(24.47)
Gestational age < 37 weeks Birth weight	475	(4.87)	85	(6.15)	72	(6.25)
Low (<2,500)	441	(4.54)	83	(6.06)	51	(4.48)
Normal (2,500–4,000)	8,581	(88.43)	1,187	(86.71)	1,000	(87.80)
High (>4,000)	682	(7.03)	99	(7.23)	88	(7.73)
Pregnancy complications <sup>b</sup>	3,225	(32.58)	487	(34.71)	434	(37.06)
5. Psychosocial characteristics						
Persistent mental health problems in pregnancy	1,145	(11.66)	185	(13.25)	167	(14.65)
Poor spousal support/ no partner	976	(9.93)	183	(13.34)	167	(15.71)
Pregnancy perceived as a difficult period	1,409	(14.29)	264	(19.02)	186	(17.45)
6. Postnatal characteristics		•				
Childcare arrangement (0–1 year)						
Parents	2,940	(30.89)	539	(40.65)	597	(56.91)
Informal (e.g., grandparents, other)	473	(4.97)	110	(8.30)	49	(4.67)
				-		

# Table 1. Characteristics of Children Participating in the ELFE Study at Age 2 (France, 2011–2013, N = 12,719) According to Maternal Immigrant Status; Information on Immigrant Status Was Missing for N = 245 Participants

(Continues)

#### Table 1. Continued

	Nonimmigrant French		Second generation immigrant		First generation immigrant	
	N	(%)	N	(%)	N	(%)
Child minder (e.g., employé à domicile, assistante						
maternelle)	4,566	(47.97)	426	(32.13)	212	(20.21)
Crèche	1,539	(16.17)	251	(18.93)	191	(18.21)
Screen exposure at age 1 year						
Often	1,259	(13.07)	311	(23.16)	375	(35.11)
Sometimes	2,603	(27.02)	423	(31.50)	341	(31.93)
Rarely or never	5,772	(59.91)	609	(45.35)	352	(32.96)
7. Multiple language exposure	899	(9.08)	569	(40.56)	911	(77.80)
Neuro- and lexical development						
Recommended M-CHAT cut offs						
Low risk (M-CHAT $\leq$ 3)	8,051	(81.32)	1,085	(77.33)	824	(70.37)
Intermediate risk (M-CHAT 3-6)	1,797	(18.15)	306	(21.81)	338	(28.86)
High risk (M-CHAT ≥ 7)	52	(0.53)	12	(0.86)	9	(0.77)
Lowest decile of MB-CDI	1,014	(10.24)	141	(10.05)	134	(11.44)
	Mean	(SD)	Mean	(SD)	Mean	(SD)
M-CHAT score, range 0-23	1.48	(1.38)	1.64	(1.42)	1.87	(1.62)
MacArthur-Bates CDI score, range 0–100	72.87	(25.14)	73.16	(24.97)	70.05	(25.26)

Abbreviation: SD, standard deviation.

<sup>a</sup>1 = no schooling, primary school, junior high school, vocational training < high school; 2 = high school degree; 3 = tertiary education.

<sup>b</sup>At least one of the following complications: hospitalization during pregnancy, risk of premature labor with or without hospitalization, premature rupture of membranes, bleeding during the second or the third trimester of pregnancy (placenta previa or placenta abruption), hypertension with concurrent proteinuria, gestational diabetes, intrauterine growth retardation.

scores. While the association in the overall sample disappeared after adjustment for covariates, the one in the first generation "other" group remained significant. Furthermore, our multivariate results are suggestive of a slight disadvantage in children of first generation mothers from the EU, which, however, was only borderline significant (P = 0.05). These findings remained robust after excluding children of mothers who completed questionnaires in a language other than French (N = 74).

Similar results were obtained in bivariate analyses studying M-CHAT risk groups (Table 3), particularly the "intermediate risk" group, with statistically significant increases in both the first and second generation groups. Associations varied by region of origin, with statistically significant results only in children of mothers from North Africa, "other" regions, as well as first generation mothers from French-speaking Sub-Saharan Africa. After adjustment, associations in children of first generation immigrants, especially if they came from North or French-speaking Sub-Saharan Africa, remained statistically significant. In addition, we found significant multivariate results in children of second generation immigrant mothers from North Africa.

Regarding the "high risk" M-CHAT group, we found a statistically significant increase in children whose mothers were first generation immigrants from North Africa, but this association was only observed in bivariate analyses, potentially due to limited statistical power.

Children of first generation mothers from "other" regions had significantly higher odds of being in the lowest decile of the MB-CDI in both bi- and multi-variate analyses (Table 3), as compared to those of the nonimmigrant French. Overall, we found no significant disadvantage in children of immigrant mothers from mostly francophone regions or the EU in terms of MB-CDI scores as binary measure.

When stratifying on children's MB-CDI level (Fig. 1), we found that among children of mothers who were first generation immigrants, M-CHAT scores were associated with poor lexical development. Further analyses (Table S3) revealed that this result was mainly driven by scores of children of women born in North Africa or French-speaking Sub-Saharan Africa.

#### Discussion

Investigating the relationship between maternal immigrant status and early development in children drawn from a representative population-based sample, we found that offspring of immigrant mothers, particularly those originating from North and French-speaking Sub-Saharan Africa, have average levels of language acquisition but appear more likely to show early signs of neurodevelopmental difficulties than those of nonimmigrant French mothers. These findings warrant additional research to verify whether these early warning signs later translate to confirmed diagnoses of neurodevelopmental conditions.

#### Limitations and Strengths

Our study has limitations, which should be acknowledged. First, although it is representative of children born

## Table 2. Maternal Immigrant Status and M-CHAT and MB-CDI Mean Scores in the ELFE Study Stratifying on Geographical Region of Origin (France, 2011–2013, N = 12,719); Crude and Fully Adjusted Linear Regression Models ( $\beta$ , 95% Confidence Interval, *P*-value)

		Beta coefficients (95% confidence interval)			
	Generation	Crude	Fully adjusted <sup>a</sup>		
M-CHAT sum score <i>(lower scores indicate</i>					
better neurodevelopment) (range: 0–23)					
Nonimmigrant French	-	ref (0)	ref (0)		
All regions	Second	0.17 (0.09–0.25)*, <i>P</i> < 0.001	0.09 (0.01–0.17)*, <i>P</i> = 0.034		
	First	0.39 (0.31–0.48)*, <i>P</i> < 0.001	0.19 (0.08–0.29)*, <i>P</i> < 0.001		
EU (excl. France)	Second	0.05 (-0.07-0.16), P = 0.452	0.03 (-0.09-0.15), P = 0.647		
	First	0.09 (-0.10-0.27), P = 0.363	0.06 (-0.13-0.25), P = 0.533		
North Africa	Second	0.26 (0.12–0.39)*, <i>P</i> < 0.001	0.13 (-0.01-0.26), P = 0.069		
	First	0.59 (0.43–0.74)*, <i>P</i> < 0.001	0.33 (0.16–0.49)*, <i>P</i> < 0.001		
French-speaking Sub-Saharan Africa	Second	0.29 (0.03–0.56)*, <i>P</i> = 0.032	0.12 (-0.14-0.39), P = 0.362		
	First	0.60 (0.42–0.78)*, <i>P</i> < 0.001	0.26 (0.07–0.45)*, <i>P</i> = 0.008		
"Other" regions	Second	0.22 (0.05–0.40)*, <i>P</i> = 0.013	0.18 (0.00-0.36)*, <i>P</i> = 0.048		
	First	0.24 (0.09–0.40)*, <i>P</i> = 0.002	0.11 (-0.05-0.27), <i>P</i> = 0.192		
MB-CDI sum score (higher scores indicate bet (range 0–100)	ter lexical development)				
Nonimmigrant French	-	ref (0)	ref (0)		
All regions	Second	0.26 (-1.15 - 1.66), P = 0.720	1.33(-0.10-2.76), P = 0.067		
-	First	-2.85 (-4.38 to -1.31)*, P < 0.001	0.45(-1.36-2.25), P = 0.627		
EU (excl. France)	Second	0.68 (-1.40-2.77), P = 0.521	1.02(-1.01-3.05), P = 0.325		
	First	-2.57(-5.88-0.75), P = 0.129	-3.32(-6.63-0.00), P = 0.050		
North Africa	Second	0.53(-1.86-2.92), P = 0.662	3.10(0.71-5.48)*, P = 0.011		
	First	-0.37(-3.05-2.31), P = 0.789	5.24 (2.38–8.09)*, P < 0.001		
French-speaking Sub-Saharan Africa	Second	-2.22(-7.03-2.59), P = 0.366	0.18(-4.43-4.79), P = 0.939		
	First	-2.45(-5.63-0.74), P = 0.132	$4.04(0.77-7.31)^*, P = 0.015$		
"Other" regions	Second	-0.13(-3.26-2.99), P = 0.933	-0.12(-3.16-2.92), P = 0.938		
č	First	–5.86 (–8.57 to –3.15)*, <i>P</i> < 0.001	-3.75 (-6.54 to -0.96)*, P = 0.008		

\*Denotes statistical significance at *P*-value < 0.05.

<sup>a</sup>Adjusted for *demographic characteristics* (maternal age, advanced paternal age, recruitment wave, geographical area of maternity) + *socioeconomic characteristics* (maternal employment, paternal employment) + *maternal health* (smoking, alcohol consumption, Body Mass Index) + *pregnancy and child characteristics* (child sex, parity, twin birth, prenatal visits, caesarean section, pregnancy complications, birth weight, gestational age) + *psychosocial characteristics* (persistent mental health problems in pregnancy, spousal support, pregnancy perceived as difficult period) + *postnatal characteristics* (childcare arrangements, screen exposure) + *multiple language exposure*.

in France in 2011, the ELFE study could not include the entire variety of children of immigrants. In particular, recent immigrants, those with very low socioeconomic status, or insufficient proficiency in study languages (French, English, Arabic, Turkish, Bambara, Soninke, or Wolof) probably did not participate or dropped out prematurely [Young, Powers, & Bell, 2006]. Thus, our study is biased toward immigrants from certain countries as well as those with better education and longer duration of stay. Additionally, by design, the ELFE cohort excluded very premature newborns, and parents of children with severe neurodevelopmental problems or other disabilities were probably less likely to participate [Callanan et al., 2001]. Overall, these excluded groups are very small, but the association between parental immigrant status and children's neurodevelopmental difficulties may nevertheless be stronger than we report. Second, we did not have access to detailed information on parents' birth country, and examined broader regions of origin, which only roughly capture diverse circumstances in terms of conflict, human development, culture, and language. Similarly, the distinctions between francophone and non-francophone regions are approximate (i.e., some countries such as Cameroon [classified as Frenchspeaking Sub-Saharan Africa] or Belgium [classified as EU] are characterized by several official languages)-vet it is likely that persons from those countries who migrate to France speak French. Third, maternal reports of children's development may be influenced by cultural differences in understanding of questionnaire items and perceptions of optimal child development. According to a systematic review, cultural adaptations of ASD screening instruments are frequently limited to language translation and rarely involve adjustments to take into account beliefs, values, and norms of the adapted culture [Al Maskari, Melville, & Willis, 2018]. However, there is also evidence suggesting that the M-CHAT is well-suited for crosscultural use. For example, in a study conducted in nine Arab countries, the M-CHAT showed a similar test performance to Western contexts [Seif Eldin et al., 2008] and in

# Table 3. Maternal Immigrant Status and M-CHAT and MB-CDI Risk Levels in the ELFE Study Stratifying on Geographical Region of Origin (France, 2011–2013, N = 12,719); Unordered Multinomial Logistic and Logistic Regression (OR, 95% Confidence Interval, *P*-value)

		Odds ratios (95% confidence interval)			
	Generation	Crude	Fully adjusted <sup>a</sup>		
М-СНАТ		Intermediate risk vs. low risk			
Nonimmigrant French	-	ref (1)	ref (1)		
All regions	Second	$1.27 (1.10-1.45)^*, P = 0.001$	1.13 (0.97–1.31), <i>P</i> = 0.112		
	First	1.82 (1.59–2.09)*, P < 0.001	1.40 (1.17–1.66)*, <i>P</i> < 0.001		
EU (excl. France)	Second	1.05(0.85-1.30), P = 0.641	1.01 (0.81–1.25), <i>P</i> = 0.959		
	First	1.27 (0.92 - 1.74), P = 0.147	1.19 (0.85–1.67), <i>P</i> = 0.301		
North Africa	Second	1.50 (1.20–1.87)*, <i>P</i> < 0.001	$1.27 (1.00 - 1.60)^*, P = 0.049$		
	First	2.34 (1.86-2.93)*, P < 0.001	1.73 (1.33–2.25)*, <i>P</i> < 0.001		
French-speaking Sub-Saharan Africa	Second	1.25(0.79-1.99), P = 0.335	1.01(0.62-1.62), P = 0.983		
	First	2.14 (1.64–2.81)*, <i>P</i> < 0.001	$1.43(1.06-1.94)^*, P = 0.019$		
"Other" regions	Second	1.39 (1.03–1.87)*, P = 0.032	1.28 (0.94–1.74), <i>P</i> = 0.119		
-	First	$1.53(1.20-1.96)^*, P = 0.001$	1.27(0.97-1.67), P = 0.086		
		High risk vs. low risk	. ,		
Nonimmigrant French	-	ref (1)	ref (1)		
All regions	Second	1.68 (0.89 - 3.18), P = 0.108	1.31(0.65-2.65), P = 0.450		
	First	1.82(0.91-3.62), P = 0.089	0.90(0.37-2.20), P = 0.818		
EU (excl. France)	Second	1.29(0.46-3.60), P = 0.623	1.31(0.45-3.78), P = 0.622		
	First	1.71(0.41-7.05), P = 0.461	2.04 (0.45 - 9.21), P = 0.354		
North Africa	Second	1.76(0.63-4.89), P = 0.278	1.00(0.33-3.02), P = 0.995		
	First	$3.46(1.38-8.72)^*, P = 0.008$	1.31(0.42-4.05), P = 0.642		
French-speaking Sub-Saharan Africa	Second	3.61(0.86-15.10), P = 0.079	2.33(0.52-10.53), P = 0.271		
	First	1.34(0.19-9.67), P = 0.768	0.42 (0.05 - 3.36), P = 0.415		
"Other" regions	Second	1.62(0.39-6.72), P = 0.503	1.50(0.35-6.49), P = 0.588		
-	First	0.63(0.09-4.56), P = 0.644	0.41 (0.05–3.29), <i>P</i> = 0.401		
MB-CDI		Lowest decile vs. upper 89%			
Nonimmigrant French	-	ref (1)	ref (1)		
All regions	Second	0.98 (0.82 - 1.18), P = 0.855	0.94 (0.77–1.15), <i>P</i> = 0.527		
-	First	1.14 (0.94–1.38), <i>P</i> = 0.182	0.97 (0.76 - 1.24), P = 0.825		
EU (excl. France)	Second	1.00 (0.76–1.31), <i>P</i> = 0.973	0.99 (0.74–1.32), <i>P</i> = 0.953		
	First	1.12 (0.74–1.69), <i>P</i> = 0.601	1.29 (0.83–2.03), <i>P</i> = 0.259		
North Africa	Second	1.04 (0.76–1.41), <i>P</i> = 0.822	0.88 (0.63 - 1.23), P = 0.444		
	First	0.77 (0.52–1.15), <i>P</i> = 0.201	$0.56 (0.36-0.87)^*, P = 0.010$		
French-speaking Sub-Saharan Africa	Second	0.92 (0.48–1.75), <i>P</i> = 0.803	0.84 (0.43 - 1.65), P = 0.618		
	First	1.12(0.74-1.68), P = 0.593	0.77 (0.49 - 1.20), P = 0.246		
"Other" regions	Second	0.89 (0.58–1.36), <i>P</i> = 0.577	0.93 (0.60–1.45), <i>P</i> = 0.750		
3	First	1.57 (1.16-2.13)*, <i>P</i> = 0.003	1.47 (1.04–2.08)*, <i>P</i> = 0.030		
		· · ·			

\*Denotes statistical significance at *P*-value < 0.05.

<sup>a</sup>Adjusted for *demographic characteristics* (maternal age, advanced paternal age, recruitment wave, geographical area of maternity) + *socioeconomic characteristics* (maternal employment, paternal employment) + *maternal health* (smoking, alcohol consumption, Body Mass Index) + *pregnancy and child characteristics* (child sex, parity, twin birth, prenatal visits, caesarean section, pregnancy complications, birth weight, gestational age) + *psychosocial characteristics* (persistent mental health problems in pregnancy, spousal support, pregnancy perceived as difficult period) + *postnatal characteristics* (childcare arrangements, screen exposure) + *multiple language* exposure.

a US-based study, the positive predictive value (PPV) did not differ by ethnicity [Herlihy, 2014], which is reassuring. Nevertheless, there is evidence that immigrant parents from certain ethnic groups tend to perceive emotional and behavioral problems in their children as less problematic [Bevaart et al., 2014]. In line with this, mothers from North and French-speaking Sub-Saharan Africa in our study might be more positive about their children's language development, potentially leading to higher MB-CDI scores. However, if present, we would expect such cultural differences to be similar across different measures, which strengthens the validity of the higher M-CHAT scores observed in the groups that also reported better language development, as measured by MB-CDI. Fourth, the PPVs of the M-CHAT are rather low, particularly when follow-up interviews are not conducted [0.11 for any DSM-IV diagnosis + developmental concerns; Chlebowski et al., 2013], and it is likely that what is captured by the measures used is overall neurodevelopment rather than ASD risk. Fifth, measures of maternal mental health and psychological distress could be affected by cultural reporting bias. Women of certain



**Figure 1.** Maternal immigrant status and M-CHAT mean scores in the ELFE study stratifying on MB-CDI scores (lowest 10% vs. highest 89%) (France, 2011–2013, N = 12,719); crude and fully adjusted linear regression models ( $\beta$ , Confidence Interval). <sup>†</sup>Adjusted for *demo-graphic characteristics* (maternal age, advanced paternal age, recruitment wave, geographical area of maternity) + *socioeconomic characteristics* (maternal education, maternal employment, paternal employment) + *maternal health* (smoking, alcohol consumption, Body Mass Index) + *pregnancy and child characteristics* (child sex, parity, twin birth, prenatal visits, caesarean section, pregnancy complications, birth weight, gestational age) + *psychosocial characteristics* (persistent mental health problems in pregnancy, spousal support, pregnancy perceived as difficult period) + *postnatal characteristics* (childcare arrangements, screen exposure) + *multiple language exposure*.

ethnic groups might not feel comfortable self-identifying as having "persistent psychological problems" because of mental illness-related stigma [Barke, Nyarko, & Klecha, 2011]. Moreover, maternal mental health in pregnancy was ascertained by a single item and may be incompletely assessed, raising the possibility of residual confounding. Incomplete adjustment may also have occurred when taking into account socioeconomic status, as maternal education might not reflect the same circumstances across the study sample. Immigrants may have problems with recognition of their educational attainment in France and research has shown that the economic returns of educational credentials tend to be lower in ethnic minority groups [Shavers, 2007]. It is therefore likely that the observed effect of SES is underestimated. Key strengths of our study are a large and representative sample, as well as a wide range of covariates that are frequently unavailable in register-based studies. We add to the literature by reporting on early signs of neurodevelopmental inequalities in children of immigrants at an age when children are rarely referred for specialist assessment. In addition, the use of parental reports and a population-based sample allowed us to circumvent potential referral bias based on ethnicity [Begeer et al., 2009] and to study variations in children's development in a nonclinical setting.

#### Interpretation of Findings

Our results indicating that the combination of low levels of language acquisition and high M-CHAT scores is more

likely to occur in children of immigrant than nonimmigrant mothers, and that this excess risk varies according to the mother's region of origin, is concordant with prior studies based on clinical diagnoses [Abdullahi et al., 2018; Crafa & Warfa, 2015; Dealberto, 2011; Kawa et al., 2017; Ng & de Montigny, 2017]. Of note, after adjustment for covariates we found that children of first generation North African or francophone Sub-Saharan African mothers had higher MB-CDI mean scores than their nonimmigrant French counterparts. Extending these prior data, our study suggests that differences in child neurodevelopment are observed both in children of first and, to a lesser degree, second generation immigrant women, implying transgenerational effects of migration on offspring neurodevelopment.

To our surprise, on average, children of immigrant mothers, particularly those originating from francophone regions, had similar levels of language acquisition to children of nonimmigrants. It may be that children's performance on the MB-CDI is related to the mother's French language proficiency rather than her immigrant status. As suggested above, it may also be that immigrant women had a more positive perception of their child's language skills. Regarding M-CHAT scores, we observed marked heterogeneity depending on the mother's region of origin. High M-CHAT scores in certain immigrant groups may thus reflect risk factors related to the circumstances of migration. Differences between children of second and first generation immigrants, and between those of immigrants from French-speaking Sub-Saharan and North Africa and the EU highlight the role of exposures directly related to migration or the country of origin, in line with previous studies suggesting that neurodevelopmental risks are highest among children of recent immigrants [Magnusson et al., 2012] and immigrants originating from countries with low human development [Magnusson et al., 2012; Lehti et al., 2016]. As human development differs between countries within the world regions we assessed, we could not thoroughly consider its role in our analyses. Nevertheless, it is reasonable to assume that on average immigrants from EU countries will have been exposed to higher levels of human development premigration than those from North and Sub-Saharan Africa. Unfortunately, to date little is known about the prevalence, determinants, and phenotypes of ASD and other neurodevelopmental disorders in North [Elsabbagh et al., 2012; Hussein & Taha, 2013] and Sub-Saharan African countries [Elsabbagh et al., 2012; Franz, Chambers, von Isenburg, & de Vries, 2017], making it impossible to compare our findings to levels of difficulties observed in the countries of origin.

Our findings suggest that neurodevelopmental problems that co-occur with low lexical development are particularly common among children of first generation immigrant mothers originating from North and French-speaking Sub-Saharan Africa. These findings partially support previous evidence suggesting that parental immigrant status may be associated with specific types of neurodevelopmental impairments. For example, Becerra et al. [2014] found that associations between immigrant- and/or ethnic minority status and ASD were stronger in children with comorbid language delay. In children with no language impairment, however, risks were comparable to those of children of USborn Caucasians, with the exception of children of foreign-born Chinese, Korean, and Mexican mothers, who had a lower risk [Becerra et al., 2014]. In Sweden, Magnusson et al. [2012] found increased risks of low-functioning, and decreased risks of high-functioning, autism in children of immigrant parents.

What are the mechanisms that may explain the excess risk of neurodevelopmental problems in children of immigrants? While many known risk factors are elevated in children of immigrant mothers, they do not fully explain this association. In our study, the greatest changes in coefficients occurred after adjustment for socioeconomic status and selected postnatal characteristics, but no excess risk was attributable to maternal health, psychosocial characteristics, or pregnancy and child characteristics, including pregnancy complications. This is partially in line with previous studies, which also found that established risk factors such as obstetrical complications do not fully explain the association between parental immigrant status and offspring ASD risk [Magnusson et al., 2012]. Similarly, our findings were not explained by children's multiple language exposure,

which is also consistent with other studies [De Houwer, Bornstein, & Putnick, 2014; Uljarević et al., 2016]. Childcare arrangements and screen use time may vary across cultural groups, potentially leading to differences in child stimulation, which is an important determinant of healthy child development [Gomajee et al., 2018; Rutter, 1998]. In a Chinese study, 3-6-year-olds with  $\geq 2$  hr of screen time scored significantly higher on the Clancy Autism Behavior Scale [Wu et al., 2017]. However, a population-based study from the United States failed to find differences in screen use time between children with and without ASD [Montes, 2016]. Of note, children in both studies were much older than our sample and it could be that intensive screen exposure is more harmful at younger ages. On the other hand, attendance of highquality center-based early childcare has been associated with positive cognitive outcomes, including better language development [Côté et al., 2013], and lower risks of emotional, behavioral and peer-relationship problems [Gomajee et al., 2018]. These benefits may be conferred by increased opportunities for cognitive stimulation and socialization, for example, in the context of structured play and reading [Gomajee et al., 2018]. Importantly, it must be noted that the causal direction of some associations in our study is not clear. For example, it could be that some children who are mainly cared for by their parents develop differently because of differences in stimulation. At the same time, children with special needs might be less likely to participate in daycare because of their disability [Benjamin, Lucas-Thompson, Little, Davies, & Khetani, 2017]. There may be factors which our study did not take into account, such as parent-child interactions, which could be less stimulating or more negative in socially isolated and socioeconomically disadvantaged families [Kiernan & Huerta, 2008]. Additionally, negative life events and lack of social support could increase maternal allostatic load and chronic stress [Keenan, Hipwell, Class, & Mbayiwa, 2018; Lecompte, Richard-Fortier, & Rousseau, 2017; van den Bergh et al., 2017], which might negatively affect brain development from pregnancy onward.

#### Conclusions

Our study provides new evidence regarding the existence of an association between maternal immigrant status and early signs of neurodevelopmental difficulties in children, particularly among those of women originating from North Africa and French-speaking Sub-Saharan Africa. Overall, these associations are stronger among children of first than second generation immigrants. Further indepth research is necessary to establish whether this association is long lasting and to unearth the underlying mechanisms, which may include life circumstances prior to and post-migration.

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#### **Conflict of Interest**

The authors declare that they have no conflict of interest.

#### Data Availability Statement

The data that support the findings of this study are available from the ELFE team (https://www.elfe-france.fr/). Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the authors with the permission of the ELFE team.

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#### **Supporting Information**

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Table S1:** Maternal immigrant status and M-CHAT and MB-CDI mean scores in the ELFE study stratifying on geographical region of origin (France, 2011–2013, N = 12,719); crude (Model 0) and sequentially adjusted (Model 1 – Model 7) linear regression models ( $\beta$ , Confidence Interval, p-value)

#### Model 0: crude association.

**Model 1:** adjusted for <u>demographic characteristics</u> (maternal age, advanced paternal age, recruitment wave, geographical area of maternity).

**Model 2:** adjusted for demographic characteristics + <u>socioeco-</u> <u>nomic characteristics</u> (maternal education, maternal employment, paternal employment).

**Model 3:** adjusted for demographic characteristics + socioeconomic characteristics + <u>maternal health</u> (smoking, alcohol consumption, Body Mass Index).

**Model 4:** adjusted for demographic characteristics + socioeconomic characteristics + maternal health + <u>pregnancy</u> <u>and child characteristics</u> (child sex, parity, twin birth, prenatal visits, caesarean section, pregnancy complications, birth weight, gestational age).

**Model 5:** adjusted for demographic characteristics + socioeconomic characteristics + maternal health + pregnancy and child characteristics + <u>psychosocial characteristics</u> (persistent mental health problems in pregnancy, spousal support, pregnancy perceived as difficult period).

**Model 6:** adjusted for demographic characteristics + socioeconomic characteristics + maternal health + pregnancy and child characteristics + psychosocial characteristics + <u>postna-</u>tal characteristics (childcare arrangements, screen exposure).

**Model 7:** adjusted for demographic characteristics + socioeconomic characteristics + maternal health + pregnancy and child characteristics + psychosocial characteristics + postnatal characteristics + <u>multiple language exposure</u>. \*Denotes statistical significance at p-value < 0.05.

**Table S2:** Characteristics of children participating in the ELFE study without *a priori* exclusion of children with incomplete maternal reports on the M-CHAT (N = 5,496) or MB-CDI (N = 5,490), and children with auditory problems at age 2 (N = 108) (France, 2011–2013, N = 18,329)

according to maternal immigrant status; information on immigrant status was missing for N = 1,587 participants

<sup> $\dagger$ </sup>1 = No schooling, primary school, junior high school, vocational training < high school; 2 = high school degree; 3 = tertiary education.

<sup>\*</sup>At least one of the following complications: hospitalization during pregnancy, risk of premature labour with or without hospitalization, premature rupture of membranes, bleeding during the second or the third trimester of pregnancy (placenta previa or placenta abruptio), hypertension with concurrent proteinuria, gestational diabetes, intrauterine growth retardation.

**Table S3:** Maternal immigrant status and M-CHAT mean scores in the ELFE study stratifying on MB-CDI scores (lowest 10% vs. highest 89%) and on geographical region of origin (France, 2011–2013, N = 12,719); crude and fully-adjusted linear regression models ( $\beta$ , Confidence Interval, p-value)

<sup>†</sup>Adjusted for <u>demographic characteristics</u> (maternal age, advanced paternal age, recruitment wave, geographical area of maternity) + <u>socioeconomic characteristics</u> (maternal education, maternal employment, paternal employment) + <u>maternal health</u> (smoking, alcohol consumption, Body Mass Index) + <u>pregnancy and child characteristics</u> (child sex, parity, twin birth, prenatal visits, caesarean section, pregnancy complications, birth weight, gestational age) + <u>psychosocial characteristics</u> (persistent mental health problems in pregnancy, spousal support, pregnancy perceived as difficult period) + <u>postnatal</u> <u>characteristics</u> (childcare arrangements, screen exposure) + multiple language exposure.

\*Denotes statistical significance at p-value < 0.05.