

## Early Onset and Increasing Disparities in Neurocognitive Delays From Birth to Age 6 in Children from Low Socioeconomic Backgrounds

Tae Hwan Han Hanyang University Seoul Hospital Kyu Young Chae CHA University School of Medicine Bo Eun Han CHA University School of Medicine Ju Hee Kim Kyung Hee University School of Medicine Eun Kyo Ha Hallym University Kangnam Sacred Heart Hospital Seonkyeong Rhie starclusters@gmail.com CHA University School of Medicine Man Yong Han CHA University School of Medicine

#### **Research Article**

#### Keywords:

Posted Date: March 5th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3997458/v1

License: (c) This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

Additional Declarations: No competing interests reported.

# Abstract Importance:

The relevance of socioeconomic conditions to neurocognitive function in children is increasingly emphasized in the current discourse; however, a comprehensive body of knowledge on this is lacking.

# Objective

To analyze the complex interplay between socioeconomic backgrounds and neurocognitive developmental achievements by investigating the temporal dynamics of these associations from birth to 6 years of age.

#### Design:

A retrospective cohort study over a 6-year period.

# Setting:

Population-based data from the National Health Insurance Service, and integrated data from the National Health Screening Program for Infants and Children.

# Participants:

Children born between 2009 and 2011 in Korea without neurocognitive delays with potential developmental implications.

# **Exposures**:

Economic status at birth, categorized into three levels based on the amount of insurance copayment: <25th percentile as low, 25-75th percentile as intermediate, and > 75th percentile as high status.

### Main Outcomes and Measures:

Overall judgement and six domains of neurocognitive development at 66–71 months of age, analyzed using the Korean Developmental Screening Test, to assess gross and fine motor function, cognition, language, sociality, and self-care. The secondary outcome was to determine when neurocognitive outcomes began after birth and how these differences evolved over time.

# Results

Among 276 167 individuals (49.2% males), 66 325 had low status, 138 980 intermediate, and 60 862 high. Overall, neurocognitive developmental delays observed across all developmental domains were more prevalent in the low-status group than in the high-status group (adjusted odds ratio, 1.328; 95% confidence interval, 1.105-1.597). Interestingly, disparities in neurocognitive development according to these statuses became apparent as early as 2 years of age, with the gap tending to widen over time (interaction, P < 0.001). Notably, the cognition and language domains exhibited the most substantial disparities between the socioeconomic levels. These disparities persisted in the subgroup analyses of sex, birth weight, head circumference, birth data, and breastfeeding variables.

#### **Conclusions and Relevance:**

Low SES was significantly associated with an increased risk of adverse neurocognitive developmental outcomes in preschool children, particularly those affecting the cognitive and language domains. These differences manifested in early childhood and tended to widen over time. Therefore, proactive interventions at a young age are essential to mitigate these disparities.

#### **Key Points**

**Question:** What are the temporal dynamics of the interplay between socioeconomic backgrounds and neurocognitive developmental achievements in children from birth to 6 years of age?

**Findings:** This retrospective cohort study found that socioeconomic status (SES) significantly influenced developmental delays in all preschool domains, with cognitive and language domains displaying the most pronounced effects. These findings remained consistent when other neurocognitive development-related factors were considered.

**Meaning:** We found that SES-related neurocognitive developmental delays were accentuated with age, highlighting the potential benefits of early screening.

#### Introduction

Neurocognitive development is profoundly shaped by the environments experienced by individuals, revealing disparities in available resources.<sup>1</sup> Various factors, including housing conditions, educational pathways, and economic well-being, comprise social status.<sup>2</sup> Socioeconomic status (SES), a key measure of social standing based on income, education, or occupation, is consistently associated with neurocognitive development from the prenatal period to adulthood. Prior investigations have highlighted the developmental delays caused by lower SES, attributing them to unequal access to essential services, goods, parental support, and social interactions. Families with higher SES tend to possess these

resources, whereas families with lower SES often face obstacles, increasing the likelihood of developmental challenges.<sup>3</sup>

Despite the significance of this issue, a comprehensive examination of neurocognitive developmental trends across the entire population has been hindered by restricted access to medical records and systemic constraints. Consequently, studies have focused on smaller cohorts within childcare facilities<sup>4</sup>; local communities<sup>5,6</sup>; or specific populations, such as premature infants.<sup>7–9</sup> Furthermore, assessments of neurocognitive development in preschool-age children have been limited, with many relying on later academic achievement as a proxy for developmental outcomes.<sup>10–12</sup> This gap in research has created a notable absence of studies encompassing extensive sample sizes representative of typical preschoolers.

Constraints in existing research may stem from the difficulty of controlling various variables that affect neurocognitive development. These variables encompass sex,<sup>13</sup> birth weight (BW),<sup>14</sup> head circumference (HC),<sup>15</sup> and the practice of breastfeeding,<sup>16</sup> all of which have been posited to be influential determinants of neurocognitive developmental trajectories. In addition, empirical evidence corroborates the significance of developmental screening assessments, which are adopted worldwide. Despite individual investigations on these aspects, a cohesive and comprehensive body of knowledge is lacking, even with the alignment of screening recommendations at analogous developmental stages.

Therefore, we investigated the intricate interplay between SES and neurocognitive development in preschool-aged children by assessing various facets of neurocognitive development, including gross and fine motor functions, cognition, language, sociality, and self-care. Additionally, we aimed to identify specific points in neurocognitive development where notable differences may emerge and determine when intervention is most crucial if significant observations are noted. This knowledge is pivotal for shaping future research initiatives, policy recommendations, and interventions to bridge neurocognitive development.

# Methods Study Design and Data Sources

This investigation analyzed healthcare resource utilization data from the National Health Insurance System (NHIS) and pertinent information from the National Health Screening Program for Infants and Children (NHSPIC).

The NHIS data encompass demographic attributes, such as date of birth, sex, insurance particulars, premium disbursements, residential location, and diagnostic codes (in accordance with the International Classification of Diseases, Tenth Revision codes).

The NHSPIC dataset, consisting of a cohort of South Korean children (n = 1 420 941) born between 2009 and 2011, underwent a meticulous six-year longitudinal examination. The NHSPIC protocol encompasses elementary inquiries and assessments, including investigations of breastfeeding practices, routine physical examinations, and evaluation of developmental milestones.

The study protocol was reviewed and approved by the Institutional Review Board of the Korea National Institute for Bioethics Policy (P01-201603-21-005). The requirement for informed consent was waived owing to the retrospective nature of this study.

# Population

Between 2009 and 2011, 1 420 941 children were born in South Korea. Figure 1 illustrates the stringent inclusion criteria applied to establish a refined cohort for analysis. The inclusion criteria were: recorded BW (n = 1 333 672), primary physical examination at 4–6 months of age (n = 796 583), completion of a 7th anthropometric assessment coupled with a neurocognitive developmental examination utilizing the Korean Infant and Toddler Ages and Stages Questionnaire (K-ASQ) or the Korean Developmental Screening Test (K-DST) (n = 699 389), and possession of pertinent health insurance premium information for the computation of SES quartiles (n = 1 367 755).

The study cohort comprised 423 836 children. Rigorous measures were undertaken to ensure the robustness of the sample, including the exclusion of participants presenting with neurocognitive delays with potential developmental implications. The exclusion criteria were: prematurity (n = 15 616), neonatal intensive care unit admission history (n = 16 399), diagnosed congenital anomalies (n = 77 034), perinatal trauma (n = 30 805), multiple births (n = 4 746), small or large gestational age (n = 79), neurologic disease (n = 24 070), deceased (n = 79), and birth trauma (n = 4 682) (Fig. 1).

# National Health Screening Program for Infants and Children

During the subject screening phase, the NHIS implemented a comprehensive series of seven iterations of the NHSPIC, targeting individuals aged 4–71 months, with specific intervals for assessments (1st, 4–6 months; 2nd, 9–12 months; 3rd, 18–24 months; 4th, 30–36 months; 5th, 42–48 months; 6th, 54–60 months; and 7th, 66–71 months). To measure neurocognitive function, the NHSPIC program used the K-ASQ as a developmental screening tool from 2008 to 2013,<sup>17–19</sup> and, in 2014, the K-DST was introduced as the primary developmental screening tool (eFigure 1). Considering the varying types of check-ups from the 2nd to the 7th iterations for neurocognitive measurement and the differing numbers of participants in each iteration, the assessment was conducted as an overall evaluation of the follow-up studies using both the K-ASQ and K-DST for secondary outcomes, whereas the main outcome utilized the 7th K-DST.

#### Exposure

SES was systematically categorized into three stratified tiers for subsequent data analysis: the lowest 25th percentile was defined as low SES, the 25th to 75th percentile as intermediate, and > 75th percentile as high.

The Korean health insurance system operates on the principles of a universal health insurance model, necessitating individuals or households to contribute monthly premiums proportionate to their respective income and wealth. Consequently, the magnitude of health insurance premiums serves as an indicator of a household's financial standing. To investigate this relationship, we isolated the premium payment component from the NHIS data.

## **Primary Outcomes**

We focused on developmental screening data derived from the 7th check-up (66–71 months of age) using the K-DST. The K-DST encompasses six domains: gross motor skills, fine motor skills, cognition, language, sociality, and self-care. Employing a comprehensive four-tiered interpretation system, the K-DST assesses developmental outcomes, categorizing them as indicative of advanced development, age-appropriate, necessitating follow-up, or warranting further evaluation.<sup>17,18</sup> Within this framework, the recommendation for further evaluation is reserved for scores falling below – 2 standard deviations.

#### Secondary Outcomes

The secondary outcome was to determine when neurocognitive function begins to show distinct characteristics influenced by socioeconomic background, and whether these differences evolve over time. To investigate this, neurocognitive assessments were conducted from the 2nd to the 7th checkups, during which the K-DST and K-ASQ were used interchangeably. Utilizing a three-tiered system, the K-ASQ categorizes outcomes as appropriate or requiring follow-up or further evaluation.<sup>19</sup>

## Covariates

We endeavored to incorporate a thorough array of subject-related information that could potentially influence developmental outcomes. Notably, variables such as HC and breastfeeding status, which were anticipated to exhibit a significant correlation with neurocognitive development, were included in our analysis because of their perceived importance.

Anthropometric indices, encompassing weight, height, body mass index (BMI), and HC, were meticulously acquired through physical measurements.<sup>20</sup> We utilized data on BW and HC values, along with the weight, height, and BMI values at the 7th check-up. Measurement precision was ensured by turning the head horizontally around the upper part of the left ear and the protruding section of the forehead while gently pressing the hair. Standardized scores (z-scores) for height, weight, BMI, and HC in male and female children of varying ages were calculated using the lambda for skew, mu for median, and sigma for the generalized coefficient of variation method. For subjects aged  $\geq$  2 years, the 2017 Korean National Growth Charts were employed,<sup>21,22</sup> while the World Health Organization growth standards were utilized for infants and young children < 2 years old.

Regarding residential status classification, children residing in metropolitan areas (Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) were designated as "metropolitan," while the remaining regions were categorized as either "city" or "rural," following the administrative divisions of the Republic of Korea. Within the scope of the variables used in our analysis, sex, BW, HC, birth year, residence, and breastfeeding status were categorized as nominal variables, whereas age, weight, height, and developmental delay were considered continuous variables.

# Statistical Analysis

Quantitative results were expressed as absolute numbers with frequencies and means with standard deviations. In exploring the association between SES and neurocognitive function, we employed a logistic regression model with adjusted odds ratios (aORs). SES, stratified into low, intermediate, and high tiers, functioned as the independent variable, while developmental delays encompassing various domains, such as gross motor skills, fine motor skills, cognition, language, sociality, and self-care, were the dependent variables. Covariate adjustments included sex, BW, HC z-score, income, birth year, and breastfeeding status. Model 2 introduced the BMI value at the 7th check-up to further refine our understanding of the SES–child development relationship.

As a secondary outcome, we employed generalized estimating equations (GEEs) to examine the evolution of developmental delays in relation to SES across multiple screening time points. The GEE, which was applied to analyze longitudinal and correlated response data, proved particularly pertinent for binary responses. SES served as the independent variable, whereas developmental delay (categorized as a recommendation for follow-up and further evaluation) was the dependent variable. Time, a continuous variable, spanned from the 2nd to the 7th check-up. Our analysis, which adjusted for covariates such as sex, birth residence, and birth year, enhanced the precision of our examination of the dynamic relationship between SES and developmental delay through multiple screenings.

We performed a subgroup analysis using logistic regression to elucidate the complex interplay between the independent variables and their influence on the probability of event occurrence. This analysis included crucial factors, such as sex, BW (above or below median average), HC z-score (above or below – 1.65), birth residence (Seoul or metropolitan, city, or rural), birth year (2008–2010 and 2011–2012), and breastfeeding at 4–6 months (breastfeeding, formula feeding, or mixed).

All statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

#### Results

### **Characteristics of Subjects**

Table 1 presents the demographic characteristics of the participants. A total of 276 167 participants were categorized into low- (66 325), intermediate- (148 980), and high-SES (60 682) groups. Notably, 51% of children born each year were female. Examination of variables such as age at the 7th checkup, BW, and HC z-score at the first checkup revealed no significant differences among the SES groups. However, significant differences were observed between the SES groups in terms of birth residence, birth year, and obesity at the 7th examination.

Table 1Basic Sociodemographic Characteristics of the Participants

Characteristic	Low SES, n (%)	Intermediate SES, n (%) (n = 148,980)	High SES, n (%) (n = 60,862)
	(n = 66,325)		
Sex			
Male	32,603 (49)	73,139 (49)	30,075 (49)
Female	33,722 (51)	75,841 (51)	30,787 (51)
Age at 7th K-DST assessment <sup>a</sup>	5.78 ± 0.19	5.79 ± 0.18	5.79 ± 0.18
Birth Weight	3.22 ± 0.33	3.22 ± 0.33	3.22 ± 0.33
HC z score at 4–6 mo. <sup>b</sup>	0.78 ± 1.25	0.80 ± 1.24	0.82 ± 1.23
Birth Residence			
Seoul	10,946 (17)	27,709 (19)	14,510 (24)
Metropolitan/City <sup>c</sup>	48,294 (73)	111,013 (75)	42,782 (70)
Rural <sup>c</sup>	5,843 (9)	9,512 (6)	3,387 (6)
Missing/Etc.	1,242 (2)	746 (1)	183 (0)
Birth year			
2009	20,307 (31)	37,837 (25)	11,599 (19)
2010	24,288 (37)	54,712 (37)	20,678 (34)
2011	21,730 (33)	56,431 (38)	28,585 (47)
Obesity at 66–72 mo. <sup>d</sup>			
Absence	59,842 (90)	136,700 (92)	56,445 (93)
Presence	6,483 (10)	12,280 (8)	4,417 (7)
BMI z score at 66–72 mo. <sup>d</sup>	0.098 ± 1.166	0.024 ± 1.120	-0.027 ± 1.092

Low	SES,	n
(%)		

<sup>a</sup> Age at 7th K-DST assessment is defined as the age of the participant at the time of the 7th checkup (66-72months).

<sup>b</sup> Obtained from the first National Health Screening Program for Infants and Children at 4–6 months after birth.

<sup>c</sup> Metropolitan areas are defined as six metropolitan cities (Busan, Incheon, Gwangju, Daejeon, Daegu, and Ulsan), cities as urban areas, and rural areas as non-city areas.

<sup>d</sup> Calculated by height and weight obtained from the first National Health Screening Program for Infants and Children at 66–72 months after birth.

Abbreviations: BMI, body mass index; HC, head circumference; K-DST, Korean Developmental Screening Test; SES, socioeconomic status

#### Main Outcome

In children who underwent the 7th K-DST, significant differences in overall neurocognitive developmental delays were observed between the high- and low-SES groups. Furthermore, meaningful differences were found across all six domains (gross motor, fine motor, cognition, language, sociality, and self-care) between the SES groups. These distinctions persisted consistently between the crude and adjusted models, except for the self-care domain, in which changes were noted with the application of the adjusted model. Specifically, the low-SES group exhibited a 32.8% (aOR, 1.328; 95% confidence interval [CI], 1.105–1.597) increased likelihood of delays in general development. The most pronounced discrepancies were evident in the cognition (aOR, 1.474; 95% CI 1.327–1.637) and language (aOR 1.455; 95% CI 1.312–1.613) domains (Table 2). Furthermore, when comparing the high- to the intermediate-SES group, discernible differences were evident. These differences, particularly in cognition (aOR, 1.036; 95% CI, 0.946–1.130) and language (aOR, 1.114; 95% CI, 1.032–1.203), remained statistically significant after adjusting for relevant factors. Notably, these disparities manifested a reduced risk compared to that of the low-SES group (Table 2).

Associations of Socioeconomic Status and Neurocognitive Development						
Characteristic	SES	Cohort	Event (%)	Crude OR (95% Cl)	aOR (Model 1) <sup>a</sup>	aOR (Model 2) <sup>b</sup>
					(95% CI)	(95% CI)
Overall	Low	65,349	976 (1.5)	1.597 (1.439– 1.772)	1.336 (1.111– 1.606)	1.328 (1.105– 1.597)
	Intermediate	147,514	1,466 (1.0)	1.063 (0.964– 1.171)	0.984 (0.859- 1.126)	0.983 (0.859– 1.125)
	High	60,298	364 (0.9)	ref	ref	ref
Gross motor	Low	64,542	1,783 (2.8)	1.388 (1.288- 1.495)	1.271 (1.116- 1.447)	1.268 (1.113- 1.444)
	Intermediate	145,779	3,201 (2.2)	1.103 (1.031– 1.180)	1.064 (0.968– 1.169)	1.063 (0.967– 1.169)
	High	59,674	1,188 (2.0)	ref	ref	ref
Fine motor	Low	64,060	2,265 (3.5)	1.506 (1.408- 1.612)	1.323 (1.174– 1.489)	1.320 (1.173- 1.487)
	Intermediate	145,209	3,771 (2.6)	1.106 (1.040- 1.177)	1.064 (0.960– 1.141)	1.046 (0.959 - 0.141)
	High	59,466	1,396 (2.3)	ref	ref	ref
Cognition	Low	63,270	3,055 (4.8)	1.730 (1.626– 1.837)	1.477 (1.330- 1.640)	1.474 (1.327– 1.637)
	Intermediate	144,102	4,878 (3.4)	1.212 (1.145- 1.282)	1.129 (1.045- 1.220)	1.219 (1.045- 1.220)

Table 2 Associations of Socioeconomic Status and Neurocognitive Development

<sup>a</sup> Model 1 is adjusted for sex, birth weight, head circumference at 4–6 months, residence at birth, income, year of birth, and breastfeeding status at 4–6 months.

<sup>b</sup> Model 2 is adjusted for Model 1 with the BMI of the 7th iteration.

Reference: high SES.

SES, socioeconomic status; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval

Characteristic	SES	Cohort	Event (%)	Crude OR (95% CI)	aOR (Model 1) <sup>a</sup>	aOR (Model 2) <sup>b</sup>
	Llinh	50.000	1 ( [ ]		(95% CI)	(95% CI)
	High	59,208	(2.8)	ret	ret	ret
Language	Low	63,174	3,151 (5.0)	1.747 (1.645- 1.856)	1.457 (1.314- 1.616)	1.455 (1.312- 1.613)
	Intermediate	143,971	5,009 (3.5)	1.219 (1.153- 1.289)	1.115 (1.033- 1.203)	1.114 (1.032- 1.203)
	High	59,173	1,689 (2.9)	ref	ref	ref
Sociality	Low	64,320	2,005 (3.1)	1.386 (1.292– 1.486)	1.217 (1.077– 1.375)	1.218 (1.078- 1.376)
	Intermediate	145,381	3,599 (2.5)	1.101 (1.033– 1.173)	1.034 (0.946- 1.129)	1.036 (0.946– 1.130)
	High	59,523	1,339 (2.2)	ref	ref	ref
Self-care	Low	64,841	1,484 (2.3)	1.198 (1.108- 1.295)	1.129 (0.983- 1.296)	1.128 (0.982– 1.295)
	Intermediate	146,163	2,817 (1.9)	1.009 (0.941– 1.081)	0.981 (0.889– 1.084)	0.981 (0.889– 1.084)
	High	59,721	1,141 (1.9)	ref	ref	ref
<sup>a</sup> Model 1 is adjusted for sex, birth weight, head circumference at 4–6 months, residence at birth, income, year of birth, and breastfeeding status at 4–6 months.						
<sup>b</sup> Model 2 is adjusted for Model 1 with the BMI of the 7th iteration.						
Reference: high SES.						

SES, socioeconomic status; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval

#### Secondary Outcome

We investigated developmental changes at successive screening intervals, beginning with the 2nd screening, encompassing developmental assessments at 9–12 months. Distinct differences by SES became apparent from the 3rd screening (18–24 months) onward. Both screenings necessitated follow-

up assessment. In the presence of an interaction between SES and time to neurocognitive delay, the analysis revealed a significant effect of time, with an estimate of 0.0864 (interaction P < 0.001). These findings persisted after adjusting for sex, place of birth, and year of birth (estimate 0.0867, interaction P-value < 0.001), as illustrated in Fig. 2.

## Subgroup Analysis

In the subgroup analyses, no discernible distinctions were observed between the high- and intermediate-SES strata across the spectrum of measured parameters. Nevertheless, in the low-SES cohort, a substantial disparity was observed in all parameters. There was a notably heightened prevalence of neurocognitive delays, regardless of SES, particularly among males, individuals born in cities and rural areas, those deprived of breastfeeding, and within the temporal window from 2011 to 2012, as shown in Fig. 3. Stratified analyses were conducted to assess the effects of these conditions on neurocognitive delays. While neurocognitive delays appeared more prevalent in specific groups within the low-SES group than those in the high-SES group, no differences were observed based on sex, BW, HC, or breastfeeding status, except for birth year, as depicted in Fig. 4.

#### Discussion

This study revealed noteworthy SES-related disparities in neurocognitive development among preschoolaged children. It is well known that children born with low SES are at an increased risk of neurocognitive delay by 6 years compared to those born with high SES.

Cognitive and language skills emerged as salient areas of distinction, although disparities were evident across all developmental domains. This aligns with the existing research that underscores the substantial influence of SES on language and cognitive development, among other facets of child development. Our findings corroborate the well-established notion that SES has a robust impact on various domains of child development. This influence persisted even after considering several influential variables, including sex, BW, HC, birth residence, parental income, year of birth, and breastfeeding status. By scrutinizing the impact of these variables on the development of our cohort, we observed parallels with previous research, such as sex, while uncovering divergences exemplified by the role of breastfeeding.

We also investigated the timeline at which SES-related developmental delays became apparent. Intriguingly, disparities were discernible as early as 9–12 months of age, coinciding with the initiation of developmental screening, and became more apparent by 18–24 months of age. This temporal analysis provides valuable insights into the trajectory of SES-related developmental differences, thereby enhancing our understanding of the critical periods during which interventions may be most impactful.

Elucidating the association between socioeconomic factors and children's development has been a persistent subject of inquiry. Substantive evidence underscores the impact of SES on overall brain development and children's behavior,<sup>23</sup> particularly in domains such as executive function and memory

ability.<sup>24–27</sup> These disparities, well-documented in the literature, are attributed to increased behavioral problems and diminished self-regulation in early childhood contingent upon SES.<sup>28</sup> The relationship between SES and cognitive development transcends geographical boundaries and economic disparities, as corroborated by extensive global statistical confirmation.<sup>29–31</sup>

Notably, lower SES has been linked to a higher prevalence of intellectual deficits among children, as evidenced the study by Chowdhury and Gosh<sup>30</sup> examining 500 children, where lower SES was associated with intellectual deficits measured through nutritional status. In post-transitional countries, SES has been identified as a pivotal determinant of developmental outcomes, even among children of average weight.<sup>31</sup> Cognitive developmental delays appear to manifest as early as infancy, with discernible differences in vocabulary and picture similarity.<sup>32</sup> These early disparities, particularly in language and cognitive domains, are precursors to broader discrepancies, including lower intelligence quotient (IQ) and divergent academic performance.<sup>4,33</sup> The pervasive influence of SES extends to language development, impacting IQ at younger ages and influencing educational achievement in the early school years.

Empirical evidence from studies conducted in the United Kingdom underscores the elevated risk of language delays among children from lower economic backgrounds. Our findings of disparities in cognitive and language development during the preschool years align with the broader body of evidence.<sup>34</sup> Critical facets of cognitive and language development influenced by SES include parental education, home environment, caregiver–child relationships, language exposure, and interactive communication dynamics. It is noteworthy that early language development plays a predictive role in later academic performance, underscoring the importance of parent–child communication.

Neuroimaging studies revealed distinct brain activity patterns in children with high- and low-SES, elucidating the neural underpinnings of cognitive and language skill disparities. Children with high SES exhibit increased activity in brain regions associated with math and language performance, while children with low SES exhibit heightened activity in areas linked to spatial processing.<sup>35</sup>

Sex-specific neurocognitive developmental outcomes have been extensively investigated, drawing insights from epidemiological, biological, cognitive, neurobiological, genetic, endocrinological, and immunological studies. The multifaceted influences of sex and sex-related attributes on neurocognitive development are shaped by intricate interactions involving biological, psychological, and sociocultural factors.<sup>13</sup> Reduced fetal growth, as indicated by BW, is not considered a direct etiological agent in neurodevelopmental delay but rather serves as an indicator of broader phenomena, such as fetal malformations, intrauterine inflammation, and conditions such as pre-eclampsia and gestational hypertension, which are more plausible contributors to neurodevelopmental challenges.<sup>14</sup> Furthermore, HC at birth serves as a surrogate measure for prenatal cerebral growth, with smaller cranial dimensions indicating an augmented risk of subsequent neurodevelopmental issues.<sup>15</sup>

Long-chain polyunsaturated fatty acids in breast milk play a pivotal role in facilitating optimal brain development, as evidenced by consistent research highlighting the advantageous impact of breastfeeding on neurological development and superior academic performance. Empirical evidence supports the increased neural volume and activity in critical brain regions associated with neurological function in breastfeed children. Additionally, breastfeeding fosters an enhanced mother–child bond, exerting a beneficial influence on neurodevelopment.<sup>16</sup> Other factors influencing neurodevelopment, such as atopic dermatitis, torticollis, and soy milk feeding, merit consideration in future studies and subgroup analyses.<sup>36–38</sup>

The outcomes presented in this study affirm the substantial influence of SES on developmental trajectories, underpinned by diverse contributing factors, including protective mechanisms and maternal dietary considerations. Notably, findings regarding breastfeeding diverge from conventional wisdom. While breastfeeding is acknowledged for its myriad advantages, a nuanced perspective must be entertained, exercising cautious optimism regarding its role in preventing developmental delays. However, this optimism is tempered by the conjecture that breastfeeding efficacy may be influenced by intricate mechanisms related to micronutrient availability and maternal nutritional status.

Developmental screening serves the critical purpose of identifying developmental delays at the earliest possible juncture and facilitating timely interventions. The present study found an elevated prevalence of developmental delays in lower-SES groups at an earlier age, accentuating the potential societal advantages of directing attention toward developmental delays in these cohorts. Countries such as South Korea and the United States have instituted comprehensive child screening systems that integrate developmental screening protocols. In the United States, developmental screening is recommended at 9, 18, and 30 months of age. While the overarching objective of this screening initiative may not be universally acknowledged, its primary objectives include augmenting the likelihood of detecting developmental delays through standardized instruments, expediting referrals for specialized assessments.<sup>39</sup>

As this study revealed SES-related disparities in the probability of developmental delays from early childhood, it underscores the potential benefits of advocating for more thorough follow-up assessments or in-depth evaluations for children in the low-SES category. This proactive strategy, extending beyond mere developmental surveillance, is of paramount importance for enabling early interventions and mitigating the protracted societal ramifications associated with developmental delays. Global implementation of such screening programs underscores their significance in addressing developmental delays and fostering timely interventions to improve long-term outcomes.

This study had the advantage of encompassing an extensive cohort, representing almost all children born in a single country, thereby ensuring a substantial and minimally biased sample. The prolonged follow-up duration, spanning approximately 6–7 years into the preschool period, facilitated a comprehensive longitudinal assessment of developmental changes. Robust statistical corrections for various known variables were implemented to bolster the reliability of the findings. However, some limitations of this study warrant further consideration. Although the study was based on extensive datasets with multiple calibration variables to mitigate selection bias, the inherent lack of numerical precision of the developmental test posed a methodological challenge. The absence of developmental data from birth to the final assessment at 66–71 months imposed constraints on the comprehensive tracking of developmental sequences. The utilization of SES values at birth may not have precisely captured changes over the 6-year study period. Additionally, reliance on parental recall for breastfeeding records introduced potential recall bias, and the transition from the K-ASQ to the K-DST as a developmental screening test may have influenced accuracy. In the absence of K-DST data, the study resorted to the K-ASQ, resulting in numerical inconsistencies despite efforts to align the results closely. Notably, the study overlooked key educational measures, such as day care or preschool attendance, which play a pivotal role in the comprehensive assessment of child development.

#### Conclusions

SES significantly influenced developmental delays in all preschool domains, with cognitive and language domains displaying the most pronounced effects. These findings remained consistent when other neurocognitive development-related factors were considered. Notably, SES-related neurocognitive developmental delays were accentuated with age, highlighting the potential benefits of early screening. Future research, such as longitudinal studies, holds promise for uncovering the underlying mechanisms and nuances of this association. Furthermore, investigations into the effectiveness of educational interventions may offer valuable insights.

#### Declarations

# **Conflict of Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

# Role of the Funder/Sponsor

The funders had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

# Funding

This research was supported by a Korea Health Technology R&D Project grant from the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (grant number: HR22C1605030022). The funder played no role in the study design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

## **Author Contribution**

Tae Hwan Han: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Original Draft, Writing - Review & Editing, Visualization, Supervision, Project administrationKyu Young Chae: Validation, SupervisionBo Eun Han: Validation, SupervisionJu Hee Kim: Validation, SupervisionEun Kyo Ha: Validation, SupervisionSeonkyeong Rhie: Conceptualization, Methodology, Validation, Formal analysis, Data Curation, Writing - Review & Editing, Visualization, Supervision, Project administrationMan Yong Han: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data Curation, Writing - Review & Editing, Visualization, Supervision, Project administration, Funding acquisitionConflicts of Interest: The authors declare no conflict of interest.

# Acknowledgements

We are grateful to the Korean healthcare system (NHIS) and well-established screening tests (NHSPIC), which allowed us to accumulate a large dataset covering nearly all ages, which allowed us to draw meaningful results.

#### References

- John CC, Black MM, Nelson CA III (2017) Neurodevelopment: the impact of nutrition and inflammation during early to middle childhood in low-resource settings. Pediatrics 139(Supplement1):S59–S71
- 2. Darin-Mattsson A, Fors S, Kåreholt I (2017) Different indicators of socioeconomic status and their relative importance as determinants of health in old age. Int J Equity Health 16(1):1–11
- 3. Conger RD, Conger KJ, Martin MJ (2010) Socioeconomic status, family processes, and individual development. J marriage family 72(3):685–704
- 4. Fernald A, Marchman VA, Weisleder A (2013) SES differences in language processing skill and vocabulary are evident at 18 months. Dev Sci 16(2):234–248
- Sarsour K, Sheridan M, Jutte D, Nuru-Jeter A, Hinshaw S, Boyce WT (2011) Family socioeconomic status and child executive functions: The roles of language, home environment, and single parenthood. J Int Neuropsychol Soc 17(1):120–132
- 6. Rindermann H, Baumeister AE (2015) Parents' SES vs. parental educational behavior and children's development: A reanalysis of the Hart and Risley study. Learn individual differences 37:133–138
- 7. Moderately preterm-born M (2013) Developmental Delay in Moderately Preterm-Born Children with Low Socioeconomic Status: Risks Multiply. J Pediatr 5:1289–1295

- Wong HS, Edwards P (2013) Nature or nurture: a systematic review of the effect of socio-economic status on the developmental and cognitive outcomes of children born preterm. Matern Child Health J 17:1689–1700
- 9. Potijk MR, de Winter AF, Bos AF, Kerstjens JM, Reijneveld SA (2015) Behavioural and emotional problems in moderately preterm children with low socioeconomic status: a population-based study. Eur Child Adolesc Psychiatry 24:787–795
- 10. Hosokawa R, Katsura T (2018) Effect of socioeconomic status on behavioral problems from preschool to early elementary school–A Japanese longitudinal study. PLoS ONE 13(5):e0197961
- 11. Hackman DA, Gallop R, Evans GW, Farah MJ (2015) Socioeconomic status and executive function: Developmental trajectories and mediation. Dev Sci 18(5):686–702
- 12. Perry LB, McConney A (2010) Does the SES of the school matter? An examination of socioeconomic status and student achievement using PISA 2003. Teachers Coll record 112(4):1137–1162
- 13. Bölte S, Neufeld J, Marschik PB, Williams ZJ, Gallagher L, Lai M-C (2023) Sex and gender in neurodevelopmental conditions. Nat Reviews Neurol 19(3):136–159
- 14. Cortese M, Moster D, Wilcox AJ (2021) Term birthweight and neurodevelopmental outcomes. Epidemiol (Cambridge Mass) 32(4):583
- Bach CC, Henriksen TB, Larsen RT, Aagaard K, Matthiesen NB (2020) Head circumference at birth and school performance: a nationwide cohort study of 536,921 children. Pediatr Res 87(6):1112– 1118
- 16. Horta BL, de Sousa BA, de Mola CL (2018) Breastfeeding and neurodevelopmental outcomes. Curr Opin Clin Nutr Metab Care 21(3):174–178
- 17. Cheol Seong S, Kim Y-Y, Khang Y-H et al (2017) Data resource profile: the national health information database of the National Health Insurance Service in South Korea. Int J Epidemiol 46(3):799–800
- 18. Kim D, Choe YJ, Durrani BAZ, Kim E, Byeon J, Eun B-L (2023) Korean Developmental Screening Test for Infants and Children (K-DST): development, applications, and implications for future early childhood development interventions. Clin Experimental Pediatr 66(7):288
- Eun BL, Chung HJ, Cho S et al (2014) The Appropriateness of the Items of Korean Ages and Stages Questionnaires (K-ASQ) Developmental Screening Test in Korean Infants and Children. J Korean Child Neurol Soc 22(2):29–41
- 20. Kim JH, Lee JE, Shim SM et al (2021) Cohort profile: national investigation of birth cohort in Korea study 2008 (NICKs-2008). Clin Experimental Pediatr 64(9):480
- 21. Kim JH, Yun S, Hwang S-s et al (2018) The 2017 Korean National Growth Charts for children and adolescents: development, improvement, and prospects. Korean J Pediatr 61(5):135
- 22. Kwon Y, Jeong SJ (2019) Association between Body Mass Index and Hepatitis B antibody seropositivity in children. Korean J Pediatr 62(11):416
- 23. Weiland C, Yoshikawa H (2014) Does higher peer socio-economic status predict children's language and executive function skills gains in prekindergarten? J Appl Dev Psychol 35(5):422–432

- 24. Lawson GM, Hook CJ, Farah MJ (2018) A meta-analysis of the relationship between socioeconomic status and executive function performance among children. Dev Sci 21(2):e12529
- 25. Raver CC, Blair C, Willoughby M (2013) Poverty as a predictor of 4-year-olds' executive function: new perspectives on models of differential susceptibility. Dev Psychol 49(2):292
- 26. Noble KG, Houston SM, Brito NH et al (2015) Family income, parental education and brain structure in children and adolescents. Nat Neurosci 18(5):773–778
- Markant J, Ackerman LK, Nussenbaum K, Amso D (2016) Selective attention neutralizes the adverse effects of low socioeconomic status on memory in 9-month-old infants. Dev Cogn Neurosci 18:26– 33
- 28. Al-Mekhlafi HM, Mahdy MA, Sallam AA et al (2011) Nutritional and socio-economic determinants of cognitive function and educational achievement of Aboriginal schoolchildren in rural Malaysia. Br J Nutr 106(7):1100–1106
- 29. Ghosh S, Chowdhury SD, Chandra AM, Ghosh T (2015) Grades of undernutrition and socioeconomic status influence cognitive development in school children of K olkata. Am J Phys Anthropol 156(2):274–285
- Chowdhury SD, Ghosh T (2010) Nutritional and socioeconomic status in cognitive development of Santal children of Purulia district, India. Ann Hum Biol 38(2):188–193
- 31. Galván M, Uauy R, Corvalán C, López-Rodríguez G, Kain J (2013) Determinants of cognitive development of low SES children in Chile: A post-transitional country with rising childhood obesity rates. Matern Child Health J 17:1243–1251
- 32. Von Stumm S (2012) You are what you eat? Meal type, socio-economic status and cognitive ability in childhood. Intelligence 40(6):576–583
- 33. Hoff E (2013) Interpreting the early language trajectories of children from low-SES and language minority homes: implications for closing achievement gaps. Dev Psychol 49(1):4
- 34. Letts C, Edwards S, Sinka I, Schaefer B, Gibbons W (2013) Socio-economic status and language acquisition: children's performance on the new Reynell Developmental Language Scales. Int J Lang communication disorders 48(2):131–143
- 35. Demir-Lira ÖE, Prado J, Booth JR (2016) Neural correlates of math gains vary depending on parental socioeconomic status (SES). Front Psychol 7:892
- 36. Kim JH, Yi YY, Ha EK, Cha HR, Han MY, Baek H-S (2023) Neurodevelopment at 6 years of age in children with atopic dermatitis. Allergology Int 72(1):116–127
- 37. Kim OH, Lee SW, Ha EK et al (2022) Neurodevelopmental outcomes and comorbidities of children with congenital muscular torticollis: evaluation using the National Health Screening Program for Infants and Children database. Clin Experimental Pediatr 65(6):312
- 38. Ha EK, Lee SW, Kim JH et al (2021) Neurodevelopmental outcomes in infants fed with soy formula: a retrospective, national population-based observational cohort study. J Nutr 151(10):3045–3052

 Care CTFoPH (2016) Recommendations on screening for developmental delay. CMAJ 188(8):579– 587

#### Figures



#### Flow Diagram of Study Population

Socioeconomic status (SES) is categorized into three tiers based on health insurance premiums from the National Health Insurance System data.

Abbreviations: K-DST, Korean Developmental Screening Test; SES, socioeconomic status; NICU, neonatal intensive care unit; SGA, small for gestational age; LGA, large for gestational age; CNS, central nervous system



#### Figure 2

#### Predicted Probability of Neurocognitive Developmental Delay According to Socioeconomic Backgrounds

This figure shows that in the 2nd check-up, there was no difference in neurocognitive delay between the low- and high-SES groups; however, a statistical difference emerged from the 3rd check-up and continued to grow until the 7nth check-up (time estimate, 0.0867; interaction *P*<0.001). Blue, low SES; Red, intermediateSES; and Green, high SES.





7.85

High SES

ediate SES

Interr

Low SES

0.05 (Ctrl) -

0.00

■ Birth Weight ≤ mean II Birth Weight > mean



0.20

#### Figure 3

0.05

0.00

High SES

#### Prevalence of Neurocognitive Delays with Socioeconomic Status and Covariates

Low SES

ediate SES

Inten

Prevalence of neurocognitive developmental delays (event/1 000 children) according to socioeconomic status groupsusing covariate variables: A) sex, B) birth weight, C) head circumference at 4-6 months, D) birth residence, E) birth year, and F) breastfeeding status at 4-6 months.

Abbreviations: SES, socioeconomic status

Disease	Population	OR			
Sex	4.5.1				
Male					
High	381/30,075 (12.7)	1			
Intermediate	912/73,139 (12.5)	0.971 (0.860-1.097)	<b></b>		
Low	644/32,603 (19.8)	1.536 (1.349-1.749)			
Female					
High	183/30,787 (5.9)	1			
Intermediate	554/75,841 (7.3)	1.232 (1.040-1.460)			
Low		1.582 (1.314-1.905)		· · · · · · · · · · · · · · · · · · ·	
Birth Weight					
mean >=					
High	295/33,291 (8.9)	1			
Intermediate	755/81,288 (9.3)	1.047 (0.913-1.200)		-	
Low	561/36,442 (15.4)	1.668 (1.443-1.929)			
mean <	00007 574 (0.0)				
High	269/27,571 (9.8)	1			
Intermediate	/11/67,692 (10.5)	1.065 (0.924-1.228)			
Low				<del></del>	
Head circumference z score					
-1.05 <=	F 10/50 005 (0 1)				
High	548/58,295 (9.4)	1 000 (0 000 1 1 10)		22	
Intermediate	1,390/141,815 (9.8)	1.038 (0.939-1.148)		1	
LOW	911/62,692 (14.5)	1.511 (1.355-1.684)		<b>—</b>	
-1.05 >	1010 154 (0.5)				
High	10/2,451 (0.5)	1 520 (0 876 2 702)		_	
Intermediate	71/0,901 (10.3)	1.539 (0.876-2.703)			7
LOW.		2.908.(1.47.1-4.924).			<del></del>
Birth residence					
Seoul or Metropolitan	240/27 620 (8 7)				
High	240/27,029 (8.7)	1 000 (0 010 1 007)			
Intermediate	000/05,592 (9.2)	1.002 (0.913-1.237)			
City or Burgh	3/9/28,5/9 (13.3)	1.552 (1.310-1.830)			
City of Rurai	222/22 050 (0.0)				
High	323/33,050 (9.8)	1 053 (0 025 1 100)		_	
Internediate	600/62,042 (10.4) 550/26 504 (45.2)	1.053 (0.925-1.199)			
By colondon year at hirth data					
By calendar year at birth date					
2008 to 2010	207/22 277 (0.2)	1			
Intermediate	002/02 540 (0.2)	1 056 (0 026 1 206)		-	
Low	623/44 505 (14.0)	1 460 (1 277 1 601)		· · · · · · · · · · · · · · · · · · ·	
2011 to 2012	023/44,395 (14.0)	1.409 (1.277-1.091)		1072	
High	267/28 585 (0.3)	1			
Intermediate	563/56 431 (10.0)	1 047 (0 002 1 214)	-		
Low	353/31 730 (16.2)	1 602 (1 427 1 002)	A.C. 17		
Feeding			• • • • • • • • • • • • • • • • • • • •		
Breast milk feeding					
High	343/32 622 (10 5)	1			
Intermediate	856/80 536 (10.6)	1 000 (0 800 1 145)			
Low	630/36 692 (17.2)	1 604 (1 403 1 835)		<b>—</b>	
Formula feeding or mixed	030/30,032 (11.2)	1.004 (1.403-1.033)			
High	215/27 375 (7.9)	1			
Intermediate	587/66 695 (8.8)	1 132 (0 967-1 326)	,	<b>—</b>	
Low	332/28 878 (11.5)	1 457 (1 223-1 736)			
- HXU	<u> </u>		1 î	1	1 1
			0.60 1.0	2.0	4.0 6.0

#### Figure 4

#### Subgroup Analysis of Children with Neurocognitive Delays

This figure shows the results of a subgroup analysis of children with neurocognitive delaysand the association between SES and the prevalence of covariates (sex, birth weight, head circumference, birth residence, year of birth, and breastfeeding status).

Reference: high SES.

Abbreviations: OR, odds ratio

#### **Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

eComponent.docx