Identification of Neurodevelopmental Transition Patterns From Infancy to Early Childhood and Risk Factors Predicting Descending Transition: A Birth Cohort Study

Takeo Kato
United Graduate School of Child Development, Hamamatsu University School of Medicine
Tomoko Nishimura
Research Center for Child Mental Development, Hamamatsu University School of Medicine
Nagahide Takahashi
Department of Child and Adolescent Psychiatry, Nagoya University Graduate School of Medicine
Taeko Harada
Research Center for Child Mental Development, Hamamatsu University School of Medicine
Akemi Okumura
Research Center for Child Mental Development, Hamamatsu University School of Medicine
Toshiki Iwabuchi
Research Center for Child Mental Development, Hamamatsu University School of Medicine
Yoko Nomura
Queens College and Graduate Center, City University of New York
Kenji J. Tsuchiya
Research Center for Child Mental Development, Hamamatsu University School of Medicine
Nori Takei (noritakei2014@outlook.jp)
Research Center for Child Mental Development, Hamamatsu University School of Medicine

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Abstract

It is unclear whether neurodevelopmental progress from infancy to early childhood remains stable. Moreover, little is known about the risk factors, if any, affecting neurodevelopmental descending transition patterns and the relationship between these patterns and later childhood adaptive behaviours. We used data of 875 children from the Hamamatsu Birth Cohort Study in Japan. Children's neurodevelopment at 18 and 32 months and adaptive behaviours at 40 months were evaluated. Perinatal factors and infant overweight status at 18 months were investigated to identify descending-transition-associated risk factors. In the latent transition analysis, ultimately, three classes were identified for each time point, resulting in nine transition patterns; among them, 10.4% of children showed descending class shifts (normal to delayed class). Such decelerated growth was predicted by maternal pre-pregnancy overweight status (odds ratio [OR] = 2.49; 95% confidence interval [CI]: 1.23, 5.02), low maternal educational history (OR = 1.20; 95% CI: 1.04, 1.36), and infant overweight status at 18 months (OR = 5.89; 95% CI: 1.26, 27.45). Children with descending transition showed poor functioning in adaptive behaviours at the age of 40 months. Interventions targeting children with risk factors for descending transition patterns may prevent decelerated growth and subsequent poor adaptive functioning.

Introduction

An understanding of the neurodevelopmental trajectories in early life provides a clue to predict developmental pathways in later life[1,2]. Neurodevelopmental delays during early infancy negatively impact childhood development[3]. Moreover, neurodevelopmental progress from infancy to early childhood may be inconsistent, and some children may show irregular transition patterns, including descending shifts or catching-up periods[4,5]. In previous studies, however, 'developmental delays' have often been arbitrarily defined, with distributional cut-offs based on single outcome domains, so that they might overlook shifts of child neurodevelopment, especially when the course is diverted from the norm. Therefore, it is critically important to define the neurodevelopmental status or subtype based on the achievement level of development at each time point to comprehend the children's neurodevelopmental transition. In addition, no prior study has comprehensively evaluated neurodevelopmental transition patterns using multiple neurodevelopmental measures.

Little is known about risk factors that may divert the developmental course from the norm into a diverted track. Hillemeier et al.[4] found that prenatal and obstetric factors such as low maternal education, low family income, and preterm birth had an increasing effect on the diverted track. However, the developmental pathways of children are also affected by postnatal factors, including physical growth, as well as biological and environmental factors[6].

The relationship between a descending course of neurodevelopment during early childhood and untoward consequences in everyday functioning, including adaptive behaviours, at a later stage has attracted attention. While this connection has already been investigated, it only exists in a high-risk sample of siblings of children with autism spectrum disorder (ASD)[7].

Hence, this study has three aims. First, in a birth cohort sample of Japanese children (18–32 months old), to apply a statistical modelling technique (latent transition analysis; LTA)[8] to identify classes with distinct transition patterns. Second, to explore risk factors, including pre-pregnancy maternal variables, environmental indicators, and infant physical growth variables, which could predispose children to specific transition patterns, especially focusing on a diversion from normal to delayed development. Third, to determine whether children with descending transition patterns show poorer performance in adaptive behaviours at a subsequent stage (age 40 months).

Methods

Ethics approval

The study protocol was approved by the Hamamatsu University School of Medicine and University Hospital Ethics Committee (Ref Nos. 17-037 and 17-037-3) and performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from each mother for her own and her infant's participation.

Participants

This study is part of the ongoing cohort study, the Hamamatsu Birth Cohort Study for Mothers and Children (HBC Study). Participants included mothers (*n* = 1,138) and their infants (*n* = 1,258) born between 24 December 2007 and 19 March 2012. The detailed recruitment procedure has been previously described[9]. The participants were determined to be a representative sample of the general Japanese population[10].

In applying the exclusion criteria, the final sample in this study comprised 875 infants and 795 mothers (Supplementary Fig. S1 353 infants who failed to participate in outcome assessments at 18 or 32 months of age (henceforth referred to as time 1 and time 2, respectively), or both, were excluded. Two infants whose mothers had passed away before their first birthdays, an infant with a birth weight less than 1,000 g, two infants diagnosed with Down syndrome, and twins and other multiple births (*n* = 25) were also excluded.

Measures

Neurodevelopment

Neurodevelopmental progress was assessed using the Mullen Scales of Early Learning (MSEL) at time 1 and time 2[11]. MSEL is a validated composite scale for ascertaining child neurodevelopment through direct testing and is composed of five domains: gross and fine motor, visual reception, and expressive and receptive language. A Japanese version of the associated T-score, with a mean of 50 and a standard deviation (SD) of 10, was used as the outcome. The detail of the T-score and procedures of the direct

testing of MSEL and retaining the reliability of assessments among clinical evaluators have been described previously[9].

Potential Risk Factors for Neurodevelopmental Transition

Risk factors associated with neurodevelopmental transition patterns in children, especially a descending pattern from time 1 to time 2, were explored. These risk factors included infant sex, premature birth (<37 weeks), small-for-gestational-age (birth weight <10th percentile for gestational age)[12], and low placenta-to-birth-weight ratio (<10th percentile)[13]. Moreover, infant overweight status at time 1 was incorporated as another risk index[14]. This variable was determined using a standardized body mass index (sBMI), which corresponded to a BMI-for-age value with a mean of 0 and an SD of 1, obtained with reference to the World Health Organization's Child Growth Standards[15]. Then, sBMI scores were dichotomised into 'overweight' (over 1 SD) and 'others'. The mother's pre-pregnancy overweight status was also included as another variable; the self-reported pre-pregnancy BMI (kg/m^2) during early pregnancy was dichotomised as 'overweight' (over 25 kg/m^2) and 'others' groups[16]. Through an interview, demographic characteristics of the parents (i.e., age, educational history, and income) were obtained.

Adaptive Behaviours

The everyday functional levels of each child were quantified using the Vineland Adaptive Behaviour Scales second edition (VABS-□) at 40 months of age. The VABS is based on a semi-structured parental interview consisting of four domains: communication, daily living, socialization, and motor skills[17]. An overall Adaptive Behaviour Composite standardized score, with a mean of 100 and an SD of 15, was used.

Statistical Analysis

Latent Transition Analysis

LTA was used to compute the latent transition probabilities which suggest the likelihood of individuals changing classes or remaining in the same class across consecutive periods[8]. LTA may compute transition probabilities at multiple time points, such as three time points; however, the precision of estimation might become inferior owing to the involvement of a multiplicative increase in parameters. Therefore, we opted for two time points (e.g., time 1 and time 2) to achieve our goal, which was to identify classes with distinct transition patterns. Prior to the main analysis, five domains of MSEL T-scores at time 1 and time 2 were set as the outcome measures through latent class analysis (LCA: Supplementary Note 1). After the best solution at each time point was identified via LCA, the transition probability by which each individual was assigned to an optimal transition pattern was computed using LTA without potential

risk factors and covariates. For the LTA procedure, a slightly modified version of the three-step approach was followed (Supplementary Note 2)[18,19]. In this approach, potential risk factors (maternal pre-pregnancy overweight status, low maternal educational history, small-for-gestational-age, and infant overweight status at time 1) and covariates (infant sex, premature birth, placenta-to-birth-weight ratio, and household income) which differed across classes at time 1 were included in the analysis (Supplementary Note 2) and examined to determine which factors would emerge as affecting transition patterns (i.e., class shifts) using multinomial logistic regression.

Transition Pattern Effect on Adaptive Behaviours

The associations of transition patterns between time 1 and time 2, especially descending transitions, with adaptive behaviours at 40 months were investigated using linear regression analysis, wherein risk factors identified in LTA were included as covariates to account for their potential confounding effects. Familial clustering was controlled for using the Huber-Sandwich method. The statistical analyses in the present study were conducted using Mplus version 8 (https://www.statmodel.com/)[20] and Stata version 14.0 (https://www.stata.com/stata14/)[21].

Results

Neurodevelopmental Transition Patterns from Infancy to Early Childhood

Table 1 shows the participants' demographic characteristics included in the analysis. In LCA, the five-class solution for both time 1 and time 2 (Supplementary Note 1 and Table S1) was chosen. Figure 1 shows the MSEL composition of the five classes identified by the LCA procedures. At time 1 (Fig. 1a), three classes within 50 ± 1 SD (i.e., leftmost to the third column in the figure) were designated as 'normal', consisting of 'High Normal' (21.9%), 'Normal' (31.8%), and 'Low Normal' (40.9%), in order from left to right. The fourth group of children (2.2%) showed a downward deviation (-2 SD) only in the Expressive Language domain (denoted as 'Expressive Language (EL)-Delayed'). The last group (3.2%) showed low scores (below -1 SD) in all five domains ('Delayed'). Similarly, three normal classes, 'High Normal' (7.8%), 'Normal' (32.9%), and 'Low Normal' (46.3%), were identified at time 2 (Fig. 1b). The fourth group (9.9%) showed scores below -1 SD in all five domains ('Delayed'). The last group (3.1%) showed markedly low scores in all five domains ('Markedly (M)-Delayed').

Table 2 shows counts and proportions for each combination of class assignments from time 1 to time 2. Only a small number of children ($n < 9$, corresponding to less than 1%) was allocated to 12 out of the 25 observable transition classes, including the descending pattern classes. Thus, the three normal classes were amalgamated at each time point and labelled as '3-Normals' to increase statistical power during relative risk estimations of children assigned to descending transition classes in comparison with baseline control classes (i.e., normal-to-normal transition patterns). Thus, the number of transition patterns was reduced to nine. Of the 875 infants included in the analyses, 737 (84.2%) were assigned to the reference transition pattern of '3-Normals to 3-Normals' at both time points, 91 (10.4%) to the

descending transition patterns (“3-Normals to Delayed” and “3-Normals to M-Delayed”), while 24 (2.8%) were assigned to the catching-up transition patterns (“EL-Delayed to 3-Normals” and “Delayed to 3-Normals”), and 23 (2.6%) were assigned to the four transition patterns of remaining in delayed classes at both time points.

Risk Factors for Transition Patterns

Table 3 shows the risk factors in infants with descending transition patterns and those in infants with the reference transition pattern. The results of the association between risk factors and catching-up and persistent delayed transition patterns are presented in Supplementary Table S2 and Note 3. Children whose mothers had a pre-pregnancy overweight status had a 2.49-fold increase in the risk of being assigned to the “3-Normals to Delayed” transition pattern than children with the reference transition pattern (odds ratio [OR]: 2.49; 95% confidence interval [CI]: 1.23, 5.02; *P* =.011). Low maternal educational history was also associated with this descending transition pattern. A 1-year decrease in maternal educational history corresponded to a 20% increase in the risk of infants being assigned to the “3-Normals to Delayed” transition pattern (OR = 1.20; 95% CI: 1.04, 1.36; *P* =.012). Overweight status at time 1 in infants was associated with being assigned to the “3-Normals to M-Delayed” transition pattern (OR = 5.89; 95% CI: 1.26, 27.45; *P* =.024). In addition, male sex (OR = 6.13; 95% CI: 1.44, 26.01; *P* =.014) and premature birth before 37 weeks (OR = 5.12; 95% CI: 1.02, 25.63; *P* =.047) were significantly associated with the “3-Normals to M-Delayed” descending transition pattern.

Transition Patterns and Adaptive Behaviour

Table 4 presents the associations between the nine transition patterns and the Adaptive Behaviour Composite standardized scores at 40 months of age. Compared with children with the reference transition pattern, children with the two descending transition patterns showed lower adaptive scores 8 months later (“3-Normals to Delayed”: coefficient = -7.88; 95% CI: -9.77, -6.00; *P* < .0001 and “3-Normals to M-Delayed”: coefficient = -13.04; 95% CI: -18.87, -7.21; *P* < .0001). Children who stayed in delayed transition classes also showed poorer levels of adaptive ability. Conversely, children who achieved the two catching-up transition patterns had no significant differences in adaptive functioning when compared with infants in the reference transition group (“EL-Delayed to 3-Normals”: *P* =.10 and “Delayed to 3-Normals”: *P* =.82).

Data Attrition

Infants who received MSEL evaluations at time 1 and 2 were included. The rate of missing data from the five MSEL domains was minimal (1.6% in total). The full information maximum likelihood (FIML)

method, a powerful tool for missing data, was used[22]. Any biases arising from the assumption of missing at random for FIML were therefore considered negligible.

Notably, characteristics (i.e., sex, birth weight, gestational age at birth, and prematurity) of infants and parental background characteristics (i.e., parental age and maternal educational history) differed between the infants included and those excluded from the analyses (Supplementary Table S3). These differences may have biased the findings. The inverse probability weighting method[23] was applied to the final model to allow for missing variations associated with these six variables. The estimates derived from the inverse probability weighting model for descending transition patterns remained statistically significant, with ORs of 2.2 (95% CI: 1.32, 3.79; *P* = .036) for maternal overweight at pre-pregnancy, 3.89 (95% CI: 1.25, 12.06; *P* = .018) for infant overweight at time 1, 4.16 (95% CI: 1.40, 12.28; *P* = .010) for male sex, and 3.86 (95% CI: 1.40, 14.33; *P* = .043) for premature birth before 37 weeks, except for maternal educational history, which had an almost identical estimation but fell just short of statistical significance (OR: 1.12; 95% CI: 0.99, 1.26; *P* = .068).

Discussion

LTA was applied to multiple neurodevelopmental measures collected from infancy to early childhood in a Japanese birth cohort sample and found that 10.4% of children were diverted from normal neurodevelopment levels (3-Normals) to lower levels, implying decelerated developmental patterns. Maternal pre-pregnancy overweight status, infant overweight status at time 1 (i.e., 18 months), and low maternal educational history were identified as risk factors associated with descending transition patterns. Further, children assigned to descending transition patterns or who remained in delayed neurodevelopmental classes from time 1 to time 2 (i.e., 32 months) demonstrated poorer adaptive functioning at 40 months. In contrast, children with catching-up transition patterns attained a normal range of adaptive functioning at 40 months.

Our study showed that 5.4% of infants (47/875) were assigned to the delayed classes at time 1 and 13.0% (114/875) to the delayed classes at time 2, indicating that there was an overall increase in the rate of delayed infants over the study period. Further, 10.4% of infants were identified as having descending transition patterns from time 1 to time 2. A previous study based on a Taiwanese nationwide sample[24] reported that the prevalence of neurodevelopmental delay from 1 to 3 years of age increased about three to four-fold, suggesting that, akin to our findings, a substantial proportion of children show a descending developmental pattern from infancy to early childhood.

Maternal pre-pregnancy overweight status was a risk factor for a descending transition pattern. This finding supports previous studies which associated maternal pre-pregnancy overweight status with motor[25], language[26], and cognitive neurocognitive developmental delay in offspring[27]. Maternal pre-pregnancy overweight status might produce a chronic systemic inflammatory ambience in both mother and foetus, with long-lasting negative consequences for neuronal development in offspring[28] by affecting insulin and leptin levels and other inflammatory markers[29].

Infant overweight status at time 1 was considered another risk factor for descending transition patterns. Overweight status in infancy is known to be related to neurodevelopmental delays[14,30], and neuroimaging research has accumulated evidence on the relationship between overweight status and structural changes in the brain[30,31]. Obesity may cause reductions in brain volume through inflammatory responses produced by adipose tissue[32]. Thus, overweight status during infancy, when brains are developing rapidly[33], may negatively impact healthy brain development and lead to descending transition patterns in early childhood.

Low maternal education was associated with the descending transition pattern. Maternal educational history appears to be associated with variables indicating poor parenting environments, including low maternal responsivity and lack of effective communication[34], and may result in more developmental differences[35]. Genetic or inherent influences may become more salient during the later stage of infancy. For example, a declining trajectory of development has frequently been reported in children with neurodevelopmental disorders such as ASD[36], and lower levels of maternal education may be a risk factor for neurodevelopmental disorders[37].

Furthermore, male sex and premature birth before 37 weeks were associated with the descending transition pattern. These variables were treated as covariates to adjust for background characteristic differences across three classes at time 1 so that they could not be considered as risk factors. Nevertheless, given that any existing confounding and risk-increasing effects in a single variable cannot be separated, there is the possibility that these two factors, in effect, may have contributed to the descending transition. Compatible with this inference, a previous study has reported that male sex and prematurity were associated with a diversion from normal to delayed development in the neurocognitive domain during age intervals similar to our study[4].

It was found that infants with descending transition patterns and persistent delays showed lower adaptive behaviour scores at 40 months of age than infants with the reference transition pattern. Our findings regarding infants with persistent delays are consistent with a previous study, which identified an association between lower neurodevelopmental scores in infancy and poorer adaptive behaviours in siblings of children with ASD[7]. To the best of our knowledge, this is the first study to demonstrate the relationship between developmental transition patterns and later adaptive behaviour in a general population sample. Given our important finding of the relationship between descending transition patterns and later poor adaptive functioning, early intervention programs focused on children with risk factors for descending transition patterns may prevent deviations from normal developmental progress and improve adaptive functioning.

This study focused on the risk factors for descending transition; however, three of the variables were found to be related to catching-up transition patterns. Approximately half of the infants (n = 24) who belonged to the delayed classes (i.e., ‘EL-Delayed’ and ‘Delayed’) at time 1 (n = 47) made the transition to normal classes (i.e., 3-Normals) at time 2, showing catching-up transition patterns (Table 2). The

variables associated with these catching-up patterns included low maternal education, small-for-gestational-age, and income. Results and inferences for catching-up and persistent delayed transition patterns are provided in Supplementary Table S2 and Note 3.

One of the main strengths of this study was that our population comprised a representative sample of infants; thus, our findings are generalizable. Second, this study examined five domains of neurodevelopment using established instruments and direct evaluations. Third, to the best of our knowledge, this study is the first to report risk factors for predicting descending transition patterns and subsequent poorer adaptive functioning in children at the early developmental stage.

However, this study has some limitations. First, the sample size was comparatively small. Among the 25 initially identified transition patterns, 12 were each composed of less than 1% of children; thus, the three normal classes were combined into a single “3-Normals” at both time points to avoid false-negative findings due to a lack of statistical power. Second, potential postnatal risk factors for predicting transition patterns were limited only to infant BMI. Further research is warranted to determine the impact of other growth-related indices for infants, including nutritional intake, interpersonal activities at early life stages, and environmental factors (i.e., living conditions and accessibility and utilization of health and social care services). Reliance on parental reports of the adaptive performance in their offspring might also have impacted the outcome measures. It is plausible that the performance of adaptive skills in children reported by parents may have been exaggerated[38]. Nevertheless, no evidence indicated that this bias occurred in combination with specific transition patterns of neurodevelopment; thereby, it is unlikely to have confounded the findings of the association between transition classes and adaptive functioning. However, there remains the possibility that our findings may be overrepresented by a subpopulation of infants, particularly, those with developmental impairments such as ASD. Acquired knowledge and information provided regarding the disorder may have influenced parents’ reporting attitudes in favour of the research questions in the present study. The results, however, remained virtually unchanged when children diagnosed with ASD at time 2 (n = 26) by paediatricians blinded to any research hypotheses were eliminated from the analyses (Supplementary Tables S4 and S5), suggesting that our findings cannot be attributed to a specific group of developmental conditions.

In conclusion, this study underscored the dynamic nature of comprehensive neurodevelopmental progress from 18 to 32 months and identified risk factors associated with descending neurodevelopmental transition patterns during this period. In this representative sample of Japanese children, 10.4% showed descending transition patterns, which were predicted by maternal pre-pregnancy overweight status, low maternal educational history, and infant overweight status at 18 months. It was also found that children with descending transition patterns had lower adaptive behaviours at 40 months. Further studies are warranted to replicate our findings using independent samples in large studies.

Declarations

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Author contributions

TK, TN, and NT conceptualized and designed the study, carried out the analyses, drafted the initial manuscript, and revised the manuscript. NT and YN critically reviewed the manuscript. KJT coordinated and supervised data collection. Material preparation and data collection were performed by TN, TH, AO, TI, and KJT. All the authors critically reviewed and approved the final version of the manuscript.

Additional information

Competing interests: The authors declare no competing interests.

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Tables

Table 1. Characteristics of participating infants and their parents.

Infants	Mean (SD)
Birth weight (g)	2957.0 (422.2)
Gestational age at birth (weeks)	39.0 (1.4)
	n (%)
Sex	
Male	432 (49.4%)
Female	443 (50.6%)
Prematurity	
<37 weeks	46 (5.3%)
≥37 weeks	829 (94.7%)
Small-for-gestational-age	
<10^{th} percentile	77 (8.8%)
10^{th}–100^{th} percentile	798 (91.2%)
Age-standardized BMI scores at 18 months	
>1 standard deviation	50 (6.1%)
<1 standard deviation	776 (93.9%)
Parents	n (%)
Maternal BMI at pre-pregnancy (kg/m^2)	
>25.0	100 (11.4%)
<25.0	775 (88.6%)
Placenta-to birth-weight ratio	
<10^{th} percentile	152 (17.7%)
10^{th}–100^{th} percentile	707 (82.3%)
	Mean (SD)
Paternal age at birth (yr)	33.5 (5.7)
Maternal age at birth (yr)	31.7 (5.0)
Paternal education (yr)	14.1 (2.6)
Maternal education (yr)	13.8 (1.8)

Household income (million JPY)	6.0 (2.7)

SD, standard deviation; BMI, body mass index; JPY, Japanese Yen.

Table 2. Transition class counts and proportions derived by latent transition analysis (*n* = 875).

			Latent class at time 2, n (%)				
			Combined 3-Normals				
			High-Normal 68 (7.8%)	Normal 288 (32.9%)	Low-Normal 405 (46.3%)	Delayed 87 (9.9%)	M-Delayed 27 (3.1%)
Latent class at time 1, n (%)	Combined 3-Normals	High-Normal 192 (21.9%)	49 (5.6%)	87 (9.9%)	56 (6.4%)	0 (0%)	0 (0%)
		Normal 278 (31.8%)	12 (1.4%)	132 (15.1%)	130 (14.5%)	0 (0%)	4 (0.5%)
		Low-Normal 358 (40.9%)	7 (0.8%)	61 (7.0%)	203 (23.2%)	74 (8.5%)	13 (1.5%)
		EL-Delayed 19 (2.2%)	0 (0%)	6 (0.7%)	9 (1.0%)	3 (0.3%)	1 (0.1%)
		Delayed 28 (3.2%)	0 (0%)	2 (0.2%)	7 (0.8%)	10 (1.1%)	9 (1.0%)

EL-Delayed, Expressive Language Delayed; M-Delayed, Markedly Delayed.

Table 3. Association between risk factors and neurodevelopmental descending transition patterns in the final model of multinomial logistic regression analysis (*n* = 765).

	Transition from 3-Normals at time 1 (765[a])		
	to 3-Normals at time 2 (681)	Delayed at time 2 (70)	Markedly Delayed at time 2 (14)
	Reference	OR [95% CI]	OR [95% CI]
Risk factors			
Maternal overweight status at pre-pregnancy	··	2.49 [1.23, 5.02]*	1.27 [0.20, 8.02]
Low maternal education (yr)	··	1.20 [1.04, 1.36]*	1.12 [0.74, 1.69]
Male sex[b]	··	1.51 [0.88, 2.60]	6.13 [1.44, 26.01]*
Small-for-gestational-age	··	1.81 [0.72, 4.53]	0.89 [0.10, 7.93]
Premature birth before 37 weeks[b]	··	1.08 [0.33, 3.50]	5.12 [1.02, 25.63]*
Infant overweight status at 18 months	··	1.49 [0.57, 3.88]	5.89 [1.26, 27.45]*
Low placenta-to-birth-weight ratio (<10th percentile)[b]	··	1.48 [0.76, 2.87]	NA
Household income (million JPY)[b]	··	0.89 [0.78, 1.01]	0.93 [0.70, 1.23]

*P < .05

OR, odds ratio; CI, confidence interval; JPY, Japanese Yen; NA, not available.

[a] In this analysis, 47 infants who had missing values for the infant's standardised body mass index at 18 months and 16 mother-infant dyads in which the mother's placental weight was missing were excluded (n = 765).

[b] Included as covariates.

Table 4. Association between neurodevelopmental transition patterns and adaptive behaviour at 40 months in linear regression analyses with covariates[a] (n = 779).

	Adaptive Behaviour Composite standardized score
	coefficient [95% CI]
Transition patterns (*n*)	
3-Normals to 3-Normals (654)	Reference
3-Normals to Delayed (67)	-7.88 [-9.77, -6.00]****
3-Normals to Markedly Delayed (13)	-13.04 [-18.87, -7.21]****
EL-Delayed to 3-Normals (14)	-2.26 [-5.04, 0.50]
Delayed to 3-Normals (9)	0.50 [-3.98, 4.99]
EL-Delayed to Delayed (3)	-11.49 [-16.9, -6.01]****
EL-Delayed to Markedly Delayed (1)	-14.13 [-15.20, -13.06]****
Delayed to Delayed (10)	-9.76 [-13.39, -6.13]****
Delayed to Markedly Delayed (8)	-17.48 [-21.77, -13.19]****

****$P < .001$

CI, confidence intervals; EL-Delayed, Expressive Language Delayed.

[a] infant sex (male), premature birth (<37 weeks), low placenta-to-birth-weight ratio (<10th percentile), household income, maternal body mass index at pre-pregnancy (>25 kg/m^2), small-for-gestational-age (<10th percentile), infant's standardised body mass index at 18 months of age (>1 SD), and maternal educational history.

Figures

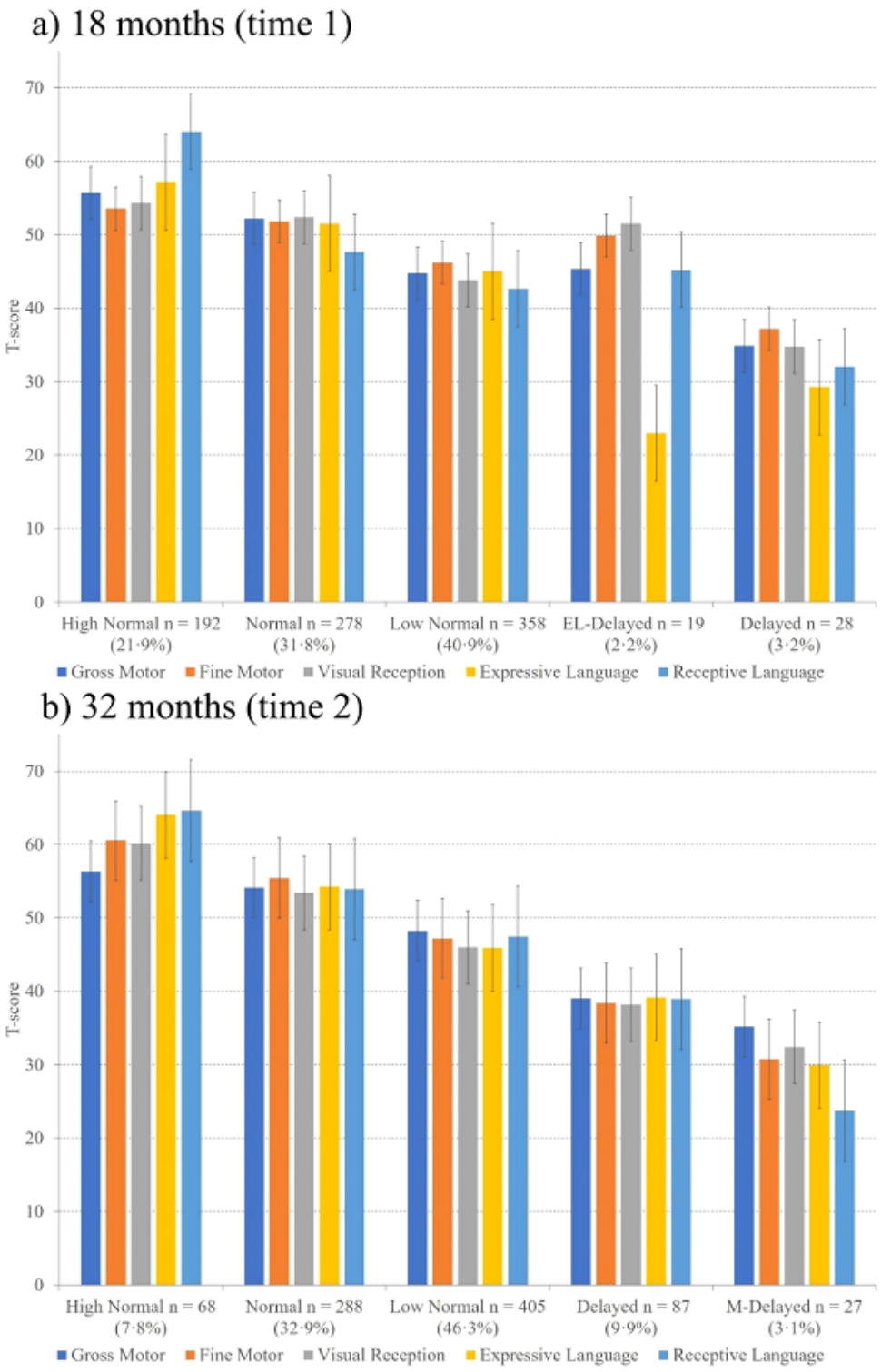

Figure 1

Latent class structure by neurodevelopmental domains at 18 months (A) and 32 months (B) (n = 875)EL-Delayed, Expressive Language Delayed; M-Delayed, Markedly Delayed.

Supplementary Files

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