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Maternal prenatal and postnatal psychological distress trajectories and impact on cognitive development in 4-year-old children: the Japan Environment and Children's Study

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Abstract

Maternal prenatal and postnatal psychological distress, including depression and anxiety, may affect children's cognitive development. However, the findings have been inconsistent. We aimed to use the dataset from the Japan Environment and Children's Study, a nationwide prospective birth cohort study, to examine this association. We evaluated the relationship between the maternal six-item version of the Kessler Psychological Distress Scale (K6) scores and cognitive development among children aged 4 years. K6 was administered twice during pregnancy (M-T1; first half of pregnancy, M-T2; second half of pregnancy) and 1 year postpartum (C-1y). Cognitive development was assessed by trained testers, using the Kyoto Scale of Psychological Development 2001. Multiple regression analysis was performed with the group with a K6 score ≤ 4 for both M-T1 and M-T2 and C-1y as a reference. Records from 1,630 boys and 1,657 girls were analyzed. In the group with K6 scores ≥ 5 in both M-T1 and M-T2 and C-1Y groups, boys had significantly lower developmental quotients (DQ) in the language-social developmental (L-S) area (partial regression coefficient: −4.09, 95% confidence interval: −6.88 – −1.31), while girls did not differ significantly in DQ for the L-S area. Among boys and girls, those with K6 scores ≤ 4 at any one or two periods during M-T1, M-T2, or C-1y did not have significantly lower DQ for the L-S area. Persistent maternal psychological distress from the first half of pregnancy to 1 year postpartum had a disadvantageous association with verbal cognitive development in boys, but not in girls aged 4 years.

Introduction

Maternal prenatal and postnatal psychological distress, including depressive symptoms and anxiety, is known to affect the children's neurodevelopment, including cognitive development, motor development, mental health, and temperament, influencing the developing fetus up to infancy (first 1000 days from conception). This process is commonly known as the "Developmental Origins of Health and Disease hypothesis."[1–4]

However, inconsistencies exist in the clinical periods from pregnancy to postpartum that are vulnerable to the effects of maternal psychological distress on children's neurodevelopment.[2,3,5] When focusing solely on the pregnancy period, reports indicated higher susceptibility in the early term, while others suggest increased susceptibility in the mid or late term of pregnancy. In a comparison between pregnancy and postpartum periods, some studies report higher susceptibility in the postpartum period than in the pregnancy period, while others find greater susceptibility during the pregnancy period than in the postpartum period.[2,3,5]

Furthermore, inconsistencies exist in the sex differences regarding vulnerability to maternal psychological distress effects on children's neurodevelopment. Generally, reports suggest boys are more susceptible than girls. Conversely, some reports show girls as more susceptible, particularly in aspects of temperament.[1,2,5]

In Japan, the Japan Environment and Children Study (JECS), a nationwide birth cohort study of approximately 100,000 pairs of parents and children, was launched in 2011.[6,7] JECS is ongoing and will continue until the participating children turn 40 years old. As a Sub-Cohort Study of the JECS, trained testers have conducted evaluations of the cognitive development of approximately 5,000 children randomly selected from the sample. In the present study, we used this dataset to evaluate the association between maternal prenatal/postnatal psychological distress trajectories and cognitive development in 4-year-old children, considering sex differences.

Methods

Design and participants

The JECS protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies (no. 100910001) and have been approved by the Ethics Committees of all participating institutions. JECS recruitment occurred between January 2011 and March 2014 and included pregnant women nationwide. Participants were recruited from 15 Regional Centers. Written informed consent was obtained from all participants. In the JECS Main Study, the eligibility criteria for participants (expecting mothers) are as follows: (1) they must reside in the study areas at the time of recruitment and are expected to continue residing in Japan for the foreseeable future; (2) they must be capable of participating in the study without difficulty, i.e., they must be able to comprehend the Japanese language and complete the self-administered questionnaire.[6]

From the JECS Main Study, a Sub-Cohort Study, which included 5% of the participating children who were randomly selected for each Regional Centre at regular intervals, was extracted.[8] The eligibility criteria were as follows: (1) children born after April 1, 2013; (2) all questionnaire and medical record data from children and their mothers collected from the first half of pregnancy to 6 months of age; and (3) biospecimens (except umbilical cord blood) from children and their mothers collected at the first to the second half of pregnancy and delivery.[8] For this Sub-Cohort Study, extended outcome measurements were planned, including face-to-face interviews with specialized staff to evaluate neurological development based on the Kyoto Scale of Psychological Development 2001 (KSPD) for 4-year-old children.[8]

The present study used the jecs-qa-20210401 dataset, which was released in April 2021 and revised in April 2023. It contains the cognitive developmental results of 4-year-old children based on the KSPD. As this study included children from singleton pregnancies, multiple-birth children were excluded. Children with congenital anomalies were also excluded from the analysis.[9] Congenital anomalies were assessed by physicians who diagnosed them immediately after delivery and during the first month at a regular checkup. Participants who had congenital anomalies reported either at delivery or at 1-month data collection were excluded from the analysis.[9]

Maternal psychological distress

The JECS administered the six-item version of the Kessler Psychological Distress Scale (K6) during the first (M-T1) and second (M-T2) half of pregnancy and at one year postpartum (C-1y). K6 is widely used to assess psychological distress during perinatal and postnatal periods.[10,11] It is a self-administered questionnaire comprising six questions that evaluate depressive mood and anxiety according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), over the preceding 4 weeks on a scale of 0 to 4. The total score is the sum of the scores of the six items, with a possible range of 0 to 24. We used a Japanese version of K6 with a cutoff score of ≥ 5 to identify cases of psychological distress, as used in previous studies of populations and affected communities in Japan.[12–15]

We analyzed the data to determine the association between K6 scores of ≥ 5 and cognitive development in 4-year-old children.

We classified participants into eight trajectory groups based on K6 scores ≥ 5 and K6 scores ≤ 4 at M-T1, M-T2, and C-1y (Table 1).

Cognitive development in 4-year-old children

The KSPD, a standardized developmental assessment tool for Japanese children, covers the cognitive-adaptive (C-A) and language-social (L-S) areas of development.[16–18] The C-A and L-S areas correspond to nonverbal and verbal cognitive development, respectively. Scores were combined to form the developmental quotient (DQ), which was calculated, in days, by dividing the developmental age in days by the chronological age and multiplying the quotient by 100. Administrative procedures and evaluations were strictly standardized to ensure tester reliability in this survey. To ensure the reliability of the administration, the testers received rigorous training before they were certified to conduct the testing. Specifically, the testers' training included general lectures by instructors, technique confirmation through watching actual examination videos, learning techniques by observing and conducting examinations, confirming correct evaluations via examination videos, and undergoing evaluation by performing examinations on mock children. The JECS and Kyoto International Social Welfare Exchange Centre certified the testers. As sex-specific differences in children's cognitive development have been suggested, we examined this issue separately for boys and girls.[2]

Statistical analysis and covariables

We compared the characteristics of mothers and their children with data on cognitive development to those obtained with an analysis of variance (ANOVA). Bivariate and multiple regression analyses were then used to assess the association between maternal psychological distress and children's cognitive development.

First, multiple regression analyses were adjusted for maternal age at delivery, whether the pregnancy was unplanned, use of infertility treatment, marital status, highest level of education (maternal and paternal), smoking during pregnancy (maternal and paternal), alcohol consumption during pregnancy, annual household income, whether the mother had any neuropsychiatric disorders, psychoactive drug use during pregnancy, pregnancy complications, obstetric labor complications, mode of delivery, children's birth weight, gestational week of delivery, feeding method at 6 months postpartum, family structure, number of children (including the subject), children's age at the time of beginning attendance at a daycare center, location of the Regional Center, and children's sex. Information regarding maternal neuropsychiatric disorders, pregnancy complications, obstetric labor complications, mode of delivery, children's birth weight, and gestational week of delivery was transcribed from physicians' records. All other information was obtained from participants' responses to the questionnaire, which was not validated. These covariate factors were mostly chosen with reference to previous

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Table 1. Characteristics of participants (total = 3287)

		Analysis set								
		Overall ($n = 3287$)		Boys ($n = 1630$)		Girls ($n = 1657$)		Reference for multiple regression analysis	Excluded ($n = 1331$)	
Variables	Category	*n*	%	*n*	%	*n*	%		*n*	%
Age of mother at the delivery (years)	Means ± SD	32.2 ± 4.8		32.2 ± 4.7		32.1 ± 4.9		continuous variable	31.4 ± 5.2	
	<20	6	0.2	5	0.3	1	0.1		9	0.7
	20–24	187	5.7	86	5.3	101	6.1		122	9.2
	25–34	2014	61.3	1000	61.4	1014	61.2		806	60.6
	≥35	1080	32.9	539	33.1	541	32.7		394	29.6
	No answer									
Unplanned pregnancy	No	3047	92.7	1508	92.5	1539	92.9	ref	1206	90.6
	Yes	240	7.3	122	7.5	118	7.1		110	8.3
	No answer								15	1.1
Parity	Primipara	1320	40.2	657	40.3	663	40.0		524	39.4
	Multipara	1922	58.5	950	58.3	972	58.7		781	58.7
	No answer	45	1.4	23	1.4	22	1.3		26	2.0
Infertility treatment	No	3040	92.5	1507	92.5	1533	92.5	ref	1230	92.4
	Yes	247	7.5	123	7.6	124	7.5		89	6.7
	No answer								12	0.9
Marital status	Married, Common-law marriage	3252	98.9	1613	99.0	1639	98.9	ref	1274	95.7
	Divorced	15	0.5	6	0.4	9	0.5		9	0.7
	Widowed	20	0.6	11	0.7	9	0.5		19	1.4
	Other								29	2.2
	No answer									
Maternal highest level of education	College/University	1503	45.7	751	46.1	752	45.4		502	37.7
	Senior high school	1695	51.6	839	51.5	856	51.7	ref	725	54.5
	Junior high school	89	2.7	40	2.5	49	3.0		83	6.2
	No answer								21	1.6
Paternal highest level of education	College/University	1423	43.3	726	44.5	697	42.1		472	35.5
	Senior high school	1700	51.7	828	50.8	872	52.6	ref	736	55.3
	Junior high school	164	5.0	76	4.7	88	5.3		88	6.6
	No answer								35	2.6
Maternal smoking during pregnancy	No	3197	97.3	1585	97.2	1612	97.3	ref	1251	94.0
	Yes	90	2.7	45	2.8	45	2.7		63	4.7
	No answer								17	1.3
Paternal smoking during pregnancy	No	2008	61.1	1011	62.0	997	60.2	ref	665	50.0
	Yes	1279	38.9	619	38.0	660	39.8		609	45.8
	No answer								57	4.3
Maternal alcohol consumption during pregnancy	No	3214	97.8	1589	97.5	1625	98.1	ref	1252	94.1
	Yes	73	2.2	41	2.5	32	1.9		41	3.1
	No answer								38	2.9

(*Continued*)

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Table 1. (*Continued*)

Variables	Category	Analysis set: Overall (*n* = 3287) *n*	%	Boys (*n* = 1630) *n*	%	Girls (*n* = 1657) *n*	%	Reference for multiple regression analysis	Excluded (*n* = 1331) *n*	%
Annual household income (×1000 yen/ year) during pregnancy	<4,000	1170	35.6	564	34.6	606	36.6	ref	466	35.0
	4,000–<6,000	1136	34.6	579	35.5	557	33.6		387	29.1
	≥6,000	981	29.8	487	29.9	494	29.8		282	21.2
	No answer								196	14.7
Maternal neuropsychiatric disorders	No	2956	89.9	1464	89.8	1492	90.0	ref	1192	89.6
	Yes	331	10.1	166	10.2	165	10.0		139	10.4
Psychoactive drugs use during pregnancy	No	3191	97.1	1584	97.2	1607	97.0	ref	1260	94.7
	Yes	96	2.9	46	2.8	50	3.0		49	3.7
	No answer								22	1.7
Pregnancy complications	No	2745	83.5	1359	83.4	1386	83.7	ref	1100	82.6
	Yes	542	16.5	271	16.6	271	16.4		208	15.6
	No answer								23	1.7
Obstetric labor complications	No	1726	52.5	846	51.9	880	53.1	ref	733	55.1
	Yes	1561	47.5	784	48.1	777	46.9		588	44.2
	No answer								10	0.8
Mode of delivery	Vaginal	2724	82.9	1353	83.0	1371	82.7	ref	1076	80.8
	Cesarean	563	17.1	277	17.0	286	17.3		248	18.6
	No answer								7	0.5
Sex of children	Boy	1630	49.6	1630	100.0				714	53.6
	Girl	1657	50.4			1657	100.0		617	46.4
Birth weigt of children (grams)	Means ± SD	3053.4 ± 396.0		3104.9 ± 408.5		3002.8 ± 376.6		continuous variable		
	0–<1500	2	0.1	1	0.1	1	0.1			
	1500–<2500	221	6.7	92	5.6	129	7.8			
	2500–<4000	3031	92.2	1512	92.8	1519	91.7			
	≥4000	33	1.0	25	1.5	8	0.5			
Gestation week of delivery	22–<34	12	0.4	4	0.3	8	0.5			
	34–<37	114	3.5	73	4.5	41	2.5			
	37–<42	3156	96.0	1552	95.2	1604	96.8	ref		
	≥42	5	0.2	1	0.1	4	0.2			
Feeding method at postpartum 6 months	Breast feeding	2104	64.0	1041	63.9	1063	64.2	ref		
	Breast feeding and infant formula	745	22.7	376	23.1	369	22.3			
	Infant formula	438	13.3	213	13.1	225	13.6			
Family structure	Extended family	614	18.7	323	19.8	291	17.6	ref		
	Nuclear family	2673	81.3	1307	80.2	1366	82.4			
Number of child included subject	1	681	20.7	350	21.5	331	20.0	ref		
	2	1719	52.3	863	52.9	856	51.7			
	≥3	887	27.0	417	25.6	470	28.4			

(*Continued*)

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Table 1. (*Continued*)

Variables	Category	Analysis set: Overall (*n* = 3287) *n*	%	Boys (*n* = 1630) *n*	%	Girls (*n* = 1657) *n*	%	Reference for multiple regression analysis	Excluded (*n* = 1331) *n*	%
Attendance at daycare center (attendance age)	Not attend	173	5.3	69	4.2	104	6.3	ref		
	0–<1	721	21.9	362	22.2	359	21.7			
	1–<2	731	22.2	366	22.5	365	22.0			
	2–<3	412	12.5	215	13.2	197	11.9			
	≥ 3	1250	38.0	618	37.9	632	38.1			
Regional Center	Hokkaido	274	8.3	135	8.3	139	8.4		116	8.7
	Miyagi	282	8.6	147	9.0	135	8.2		139	10.4
	Fukushima	411	12.5	214	13.1	197	11.9	ref	177	13.3
	Chiba	177	5.4	77	4.7	100	6.0		95	7.1
	Kanagawa	218	6.6	108	6.6	110	6.6		89	6.7
	Koshin	230	7.0	118	7.2	112	6.8		100	7.5
	Toyama	174	5.3	85	5.2	89	5.4		72	5.4
	Aichi	201	6.1	91	5.6	110	6.6		63	4.7
	Kyoto	106	3.2	54	3.3	52	3.1		55	4.1
	Osaka	255	7.8	117	7.2	138	8.3		96	7.2
	Hyogo	169	5.1	101	6.2	68	4.1		60	4.5
	Tottori	99	3.0	47	2.9	52	3.1		28	2.1
	Kochi	225	6.9	107	6.6	118	7.1		95	7.1
	Fukuoka	258	7.9	124	7.6	134	8.1		93	7.0
	South Kyusyu and Okinawa	208	6.3	105	6.4	103	6.2		53	4.0
M-T1; pregnant week	Median (IQR)	14.6 (11.9–17.9)		14.6 (12.0–18.1)		14.4 (11.9–17.7)			14.9 (12.0–18.7)	
M-T2; pregnant week	Median (IQR)	27.3 (25.1–30.0)		27.4 (25.3–30.3)		27.0 (25.1–29.9)			27.6 (25.4–30.1)	
Maternal K6; M-T1	<5	2220	67.5	1086	66.6	1134	68.4			
	5–<13	943	28.7	477	29.3	466	28.1			
	≥13	124	3.8	67	4.1	57	3.4			
Maternal K6; M-T2	<5	2390	72.7	1189	72.9	1201	72.5			
	5–<13	811	24.7	400	24.5	411	24.8			
	≥13	86	2.6	41	2.5	45	2.7			
Maternal K6; C-1Y	<5	2541	77.3	1260	77.3	1281	77.3			
	5–<13	666	20.3	330	20.3	336	20.3			
	≥13	80	2.4	40	2.5	40	2.4			

(*Continued*)

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Table 1. (*Continued*)

Variables	Category	Analysis set: Overall ($n = 3287$) *n*	%	Boys ($n = 1630$) *n*	%	Girls ($n = 1657$) *n*	%	Reference for multiple regression analysis	Excluded ($n = 1331$) *n*	%
Maternal K6; eight trajectories groups	M-T1;K6 ≤ 4 and M-T2;K6 ≤ 4 and C-1Y;K6 ≤ 4	1734	52.8	843	51.7	891	53.8	ref		
	M-T1;K6 ≤ 4 and M-T2;K6 ≥5 and C-1Y;K6 ≤ 4	198	6.0	106	6.5	92	5.6			
	M-T1;K6 ≥5 and M-T2;K6 ≤ 4 and C-1Y;K6 ≤ 4	202	6.2	102	6.3	100	6.0			
	M-T1;K6 ≥ 5 and M-T2;K6 ≥ 5 and C-1Y;K6 ≤ 4	86	2.6	35	2.2	51	3.1			
	M-T1;K6 ≤ 4 and M-T2;K6 ≤ 4 and C-1Y;K6 ≥5	331	10.1	173	10.6	158	9.5			
	M-T1;K6 ≤ 4 and M-T2;K6 ≥ 5 and C-1Y;K6 ≥ 5	127	3.9	67	4.1	60	3.6			
	M-T1;K6 ≥5 and M-T2;K6 ≤ 4 and C-1Y;K6 ≥ 5	274	8.3	142	8.7	132	8.0			
	M-T1;K6 ≥ 5 and M-T2;K6 ≥ 5 and C-1Y;K6 ≥ 5	335	10.2	162	9.9	173	10.4			
KSPD; C-A DQ	Means ± SD	96.5 ± 14.1		95.3 ± 14.7		97.6 ± 13.4				
	Minimum	24		44		24				
	25th percentile	86		84		87				
	50th percentile	97		96		99				
	75th percentile	105		105		106				
	Maximum	153		153		152				
	Skewness	0.2		0.2		0.3				
	Kurtosis	0.9		0.6		1.2				
KSPD; L-S DQ	Means ± SD	96.3 ± 15.7		95.1 ± 16.4		97.4 ± 14.9				
	Minimum	23		23		36				
	25th percentile	85		83		87				
	50th percentile	97		95		99				
	75th percentile	107		106		107				
	Maximum	147		147		144				
	Skewness	−0.1		−0.2		−0.1				
	Kurtosis	0.3		0.3		0.1				

Abbreviations: Kyoto Scale of Psychological Development 2001(KSPD), developmental quotient (DQ), cognitive-adaptive (C-A), language-social (L-S), standard deviation (SD), interquartile range (IQR), the 6-item Kessler Psychological Distress Scale (K6; total point scores ranged from 0 to 24),1 year postpartum (C-1y).

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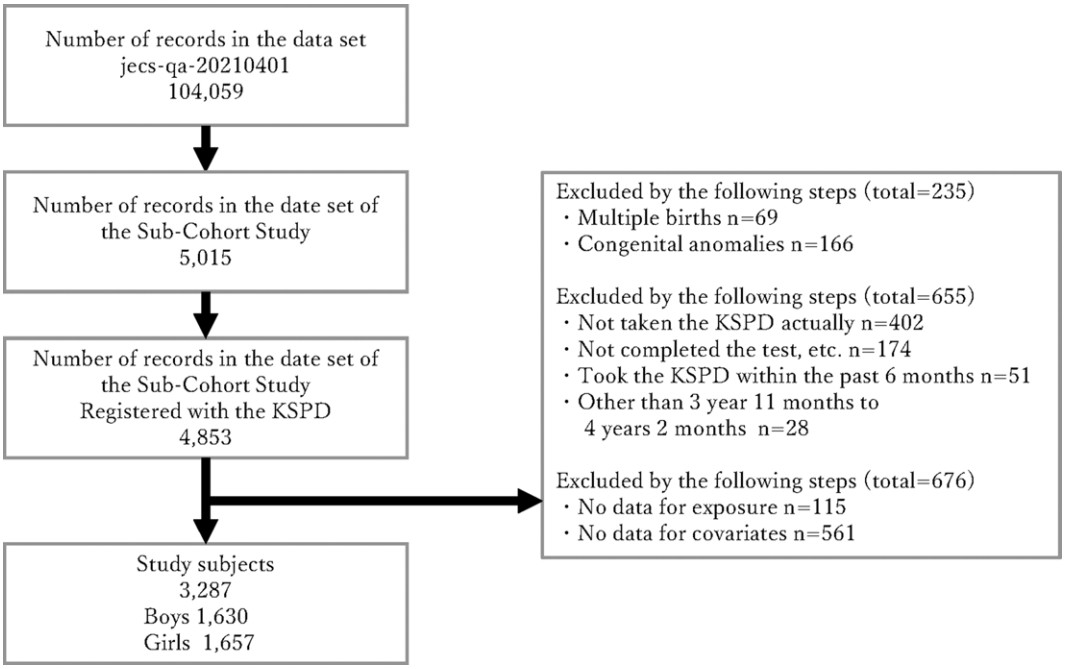

Figure 1. Flow chart depicting research participants' selection.

relevant studies.[1–4,15] No multicollinearity was found in this analysis (VIF < 2), except for parity and number of children.

Second, multiple regression analyses were adjusted for variables selected through a stepwise method, with the significance level for entry into the model set at 0.20 and for staying in the model at 0.15.

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

Results

Of the 104,059 records in this dataset, records from 3,287 children were analyzed (Fig. 1). Table 1 shows the characteristics of the participants as evaluated by the KSPD. In total, there were 1,630 boys and 1,657 girls.

In the group of boys, at M-T1, the maternal prenatal K6 score was estimated at 14.6 (interquartile range (IQR) 12.0–18.1) weeks of gestation; at M-T2, it was estimated at 27.4 (IQR 25.3–30.3) weeks of gestation. In the group of girls, at M-T1, the maternal prenatal K6 score was estimated at 14.4 (IQR 11.9–17.7) weeks of gestation; at M-T2, it was estimated at 27.0 (IQR 25.1–29.9) weeks of gestation.

Boys

The participants were divided into eight trajectory groups (Table 1). Table 2 depicts the one-way ANOVA results of maternal K6 and KSPD. Table 3 depicts the bivariate analysis of maternal K6 and KSPD.

Multiple regression analysis without the stepwise method showed significantly lower scores with maternal K6 scores ≥ 5 at both M-T1 and M-T2 and C-1y for the L-S DQ (partial regression coefficient (B): −4.09, 95% confidence interval [CI]: −6.88 – −1.31, β: −0.075, $p = 0.004$) areas, compared to those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 4). The groups with maternal K6 scores ≤ 4 at any one or two periods during M-T1, M-T2, and C-1y were not significantly different from those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 4). There were no significant differences in the C-A DQ area (Table 4).

Multiple regression analysis with the stepwise method showed significantly lower scores with maternal K6 scores ≥ 5 at both M-T1 and M-T2 and C-1y for the L-S DQ (partial regression coefficient (*B*): −3.70, 95% confidence interval [CI]: −6.41 – −0.98, *β*: −0.068, $p = 0.008$) areas, compared to those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 5). The groups with maternal K6 scores ≤ 4 at any one or two periods during M-T1, M-T2, and C-1y were not significantly different from those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 5). There were no significant differences in the C-A DQ area (Table 5).

Girls

The participants were divided into eight trajectory groups (Table 1). Table 2 depicts the one-way ANOVA results of maternal K6 and KSPD. Table 3 depicts the bivariate analysis of maternal K6 and KSPD.

Multiple regression analysis without the stepwise method showed no significant differences in maternal K6 scores ≥ 5 at both M-T1 and M-T2 and C-1y for the L-S DQ (*B*: −2.22, 95% CI: −4.60 − 0.17, *β*: −0.045, $p = 0.07$) areas, compared to maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 4). The groups with maternal K6 scores ≤ 4 at any one or two periods during M-T1, M-T2, and C-1y were also not significantly different compared to those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 4). There were no significant differences in the C-A DQ area (Table 4).

Multiple regression analysis with the stepwise method showed no significant differences in maternal K6 scores ≥ 5 at both M-T1 and M-T2 and C-1y for the L-S DQ (*B*: −2.24, 95% CI: −4.58 – 0.10, *β*: −0.046, $p = 0.06$) areas, compared to maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 5). The groups with maternal K6 scores ≤ 4 at any one or two periods during M-T1, M-T2, and C-1y were also not significantly different compared to those with maternal K6 scores ≤ 4 at both M-T1 and

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Table 2. ANOVA of Maternal K6 and KSPD in eight trajectories groups.

	Maternal K6			Overall ($n = 3287$)				Boys ($n = 1630$)				Girls ($n = 1657$)			
	M-T1	M-T2	C-1Y	*n*	%	Means ± SD	*p*	*n*	%	Means ± SD	*p*	*n*	%	Means ± SD	*p*
C-A DQ	≤4	≤4	≤4	1734	52.8	97.3 ± 14.3	0.004	843	51.7	96.1 ± 15.0	0.049	891	53.8	98.3 ± 13.5	0.20
	≤4	≤4	≥5	198	6.0	96.3 ± 13.7		106	6.5	96.7 ± 12.7		92	5.6	95.8 ± 14.8	
	≤4	≥5	≤4	202	6.2	96.1 ± 13.4		102	6.3	94.6 ± 14.4		100	6.0	97.7 ± 12.1	
	≤4	≥5	≥5	86	2.6	98.3 ± 14.5		35	2.2	97.7 ± 13.4		51	3.1	98.7 ± 15.4	
	≥5	≤4	≤4	331	10.1	96.1 ± 13.5		173	10.6	95.3 ± 14.2		158	9.5	97.0 ± 12.7	
	≥5	≤4	≥5	127	3.9	95.2 ± 12.6		67	4.1	93.8 ± 13.9		60	3.6	96.8 ± 10.8	
	≥5	≥5	≤4	274	8.3	95.1 ± 14.6		142	8.7	93.3 ± 15.6		132	8.0	97.0 ± 13.3	
	≥5	≥5	≥5	335	10.2	94.0 ± 14.3		162	9.9	92.5 ± 14.8		173	10.4	95.4 ± 13.6	
L-S DQ	≤4	≤4	≤4	1734	52.8	97.1 ± 15.7	0.001	843	51.7	96.1 ± 16.3	0.01	891	53.8	98.0 ± 14.9	0.21
	≤4	≤4	≥5	198	6.0	95.8 ± 15.2		106	6.5	95.2 ± 14.7		92	5.6	96.4 ± 15.9	
	≤4	≥5	≤4	202	6.2	96.9 ± 14.7		102	6.3	94.9 ± 15.5		100	6.0	98.9 ± 13.6	
	≤4	≥5	≥5	86	2.6	97.2 ± 14.8		35	2.2	97.9 ± 15.9		51	3.1	96.7 ± 14.1	
	≥5	≤4	≤4	331	10.1	96.8 ± 16.4		173	10.6	95.7 ± 17.2		158	9.5	97.9 ± 15.4	
	≥5	≤4	≥5	127	3.9	95.8 ± 15.1		67	4.1	93.8 ± 16.5		60	3.6	98.0 ± 13.1	
	≥5	≥5	≤4	274	8.3	94.7 ± 16.0		142	8.7	92.9 ± 16.4		132	8.0	96.8 ± 15.5	
	≥5	≥5	≥5	335	10.2	92.8 ± 15.9		162	9.9	90.9 ± 16.7		173	10.4	94.5 ± 14.9	

Abbreviations: Kessler Psychological Distress Scale (K6), Kyoto Scale of Psychological Development 2001(KSPD), developmental quotient (DQ), cognitive-adaptive (C-A), language-social (L-S), interquartile range (IQR),1 year postpartum (C-1y).
M-T1; Overall median 14.6 (IQR 11.9–17.9), Boys median 14.6 (IQR 12.0–18.1), Girls median 14.4 (IQR 11.9–17.7) pregnant week.
M-T2; Overall median 27.3 (IQR 25.1–30.0), Boys median 27.4 (IQR 25.3–30.3), Girls median 27.0 (IQR 25.1–29.9) pregnant weeks.

Table 3. Bivariate analysis of Maternal K6 and KSPD in eight trajectories groups.

	Maternal K6			Overall ($n = 3287$)							Boys ($n = 1630$)							Girls ($n = 1657$)						
	M-T1	M-T2	C-1Y	Pr > F	R^2	B	95%CI			β	p	Pr > F	R^2	B	95% CI			β	p	Pr > F	R^2	B	95% CI			β	p
C-A DQ	≤4	≤4	≤4	0.004	0.006	ref						0.049	0.009	ref						0.20	0.006	ref					
	≤4	≤4	≥5			−0.93	−3.00	–	1.14	−0.016	0.38			0.61	−2.36	–	3.58	0.010	0.69			−2.48	−5.35	–	0.40	−0.042	0.09
	≤4	≥5	≤4			−1.12	−3.17	–	0.93	−0.019	0.29			−1.55	−4.57	–	1.47	−0.026	0.31			−0.59	−3.36	–	2.17	−0.011	0.67
	≤4	≥5	≥5			1.00	−2.05	–	4.05	0.011	0.52			1.53	−3.44	–	6.50	0.015	0.55			0.34	−3.43	–	4.12	0.004	0.86
	≥5	≤4	≤4			−1.14	−2.79	–	0.52	−0.024	0.18			−0.80	−3.21	–	1.60	−0.017	0.51			−1.33	−3.59	–	0.93	−0.029	0.25
	≥5	≤4	≥5			−2.04	−4.58	–	0.49	−0.028	0.11			−2.35	−6.01	–	1.31	−0.032	0.21			−1.51	−5.00	–	1.99	−0.021	0.40
	≥5	≥5	≤4			−2.15	−3.95	–	−0.36	−0.042	0.02			−2.83	−5.44	–	−0.21	−0.054	0.03			−1.29	−3.73	–	1.16	−0.026	0.30
	≥5	≥5	≥5			−3.26	−4.91	–	−1.62	−0.070	0.0001			−3.65	−6.12	–	−1.18	−0.074	0.004			−2.91	−5.09	–	−0.73	−0.066	0.01
L-S DQ	≤4	≤4	≤4	0.001	0.008	ref						0.01	0.011	ref						0.21	0.006	ref					
	≤4	≤4	≥5			−1.30	−3.60	–	1.01	−0.020	0.27			−0.88	−4.18	–	2.42	−0.013	0.60			−1.58	−4.78	–	1.63	−0.024	0.33
	≤4	≥5	≤4			−0.21	−2.50	–	2.07	−0.003	0.85			−1.25	−4.60	–	2.11	−0.018	0.47			0.91	−2.17	–	4.00	0.015	0.56
	≤4	≥5	≥5			0.14	−3.25	–	3.54	0.001	0.93			1.84	−3.68	–	7.37	0.016	0.51			−1.27	−5.48	–	2.94	−0.015	0.55
	≥5	≤4	≤4			−0.31	−2.15	–	1.54	−0.006	0.74			−0.36	−3.03	–	2.31	−0.007	0.79			−0.11	−2.63	–	2.42	−0.002	0.93
	≥5	≤4	≥5			−1.29	−4.11	–	1.54	−0.016	0.37			−2.29	−6.36	–	1.77	−0.028	0.27			0.00	−3.90	–	3.91	0.000	1.00
	≥5	≥5	≤4			−2.33	−4.32	–	−0.33	−0.041	0.02			−3.25	−6.15	–	−0.34	−0.056	0.03			−1.21	−3.94	–	1.51	−0.022	0.38
	≥5	≥5	≥5			−4.27	−6.11	–	−2.44	−0.082	<.0001			−5.19	−7.93	–	−2.44	−0.095	0.0002			−3.43	−5.86	–	−1.00	−0.070	0.01

Abbreviations: Kessler Psychological Distress Scale (K6), Kyoto Scale of Psychological Development 2001(KSPD), developmental quotient (DQ), cognitive-adaptive (C-A), language-social (L-S), partial regression coefficient (B), confidence interval (CI), standardized partial regression coefficients (β), interquartile range (IQR),1 year postpartum (C-1y).
M-T1; Overall median 14.6 (IQR 11.9–17.9), Boys median 14.6 (IQR 12.0–18.1), Girls median 14.4 (IQR 11.9–17.7) pregnant weeks. M-T2; Overall median 27.3 (IQR 25.1–30.0), Boys median 27.4 (IQR 25.3–30.3), Girls median 27.0 (IQR 25.1–29.9) pregnant weeks.

Table 4. Multiple regression analysis of Maternal K6 and KSPD in eight trajectories groups.

	Maternal K6			Overall ($n = 3287$)							Boys ($n = 1630$)							Girls ($n = 1657$)						
	M-T1	M-T2	C-1Y	Pr > F	R^2	B	95%CI			β	p	Pr > F	R^2	B	95%CI			β	p	Pr > F	R^2	B	95%CI			β	p
C-A DQ	≤4	≤4	≤4	<.0001	0.084	ref						<.0001	0.091	ref						<.0001	0.099	ref					
	≤4	≤4	≥5			−0.66	−2.68	–	1.35	−0.011	0.52			0.77	−2.15	–	3.70	0.013	0.60			−2.25	−5.05	–	0.55	−0.039	0.11
	≤4	≥5	≤4			−0.58	−2.58	–	1.42	−0.010	0.57			−0.52	−3.51	–	2.46	−0.009	0.73			−0.57	−3.27	–	2.14	−0.010	0.68
	≤4	≥5	≥5			0.56	−2.42	–	3.53	0.006	0.71			1.17	−3.71	–	6.05	0.012	0.64			0.07	−3.64	–	3.78	0.001	0.97
	≥5	≤4	≤4			−0.73	−2.34	–	0.89	−0.015	0.38			0.08	−2.28	–	2.45	0.002	0.94			−1.26	−3.47	–	0.96	−0.028	0.27
	≥5	≤4	≥5			−1.50	−3.98	–	0.98	−0.021	0.24			−1.41	−5.06	–	2.23	−0.019	0.45			−1.28	−4.72	–	2.16	−0.018	0.47
	≥5	≥5	≤4			−0.53	−2.30	–	1.25	−0.010	0.56			−0.87	−3.49	–	1.75	−0.017	0.52			0.11	−2.32	–	2.54	0.002	0.93
	≥5	≥5	≥5			−2.00	−3.65	–	−0.35	−0.043	0.02			−1.90	−4.40	–	0.61	−0.039	0.14			−1.87	−4.06	–	0.32	−0.043	0.09
L-S DQ	≤4	≤4	≤4	<.0001	0.106	ref						<.0001	0.093	ref						<.0001	0.141	ref					
	≤4	≤4	≥5			−1.18	−3.40	–	1.04	−0.018	0.30			−0.96	−4.21	–	2.29	−0.014	0.56			−1.50	−4.55	–	1.55	−0.023	0.33
	≤4	≥5	≤4			0.35	−1.85	–	2.54	0.005	0.76			0.16	−3.16	–	3.48	0.002	0.93			0.67	−2.28	–	3.62	0.011	0.66
	≤4	≥5	≥5			−0.09	−3.36	–	3.18	−0.001	0.96			0.93	−4.50	–	6.36	0.008	0.74			−0.88	−4.92	–	3.16	−0.010	0.67
	≥5	≤4	≤4			0.07	−1.71	–	1.84	0.001	0.94			0.36	−2.27	–	3.00	0.007	0.79			−0.06	−2.47	–	2.35	−0.001	0.96
	≥5	≤4	≥5			−1.20	−3.93	–	1.53	−0.015	0.39			−1.77	−5.82	–	2.29	−0.021	0.39			−0.61	−4.35	–	3.14	−0.008	0.75
	≥5	≥5	≤4			−1.24	−3.20	–	0.71	−0.022	0.21			−1.87	−4.79	–	1.04	−0.032	0.21			−0.25	−2.90	–	2.39	−0.005	0.85
	≥5	≥5	≥5			−3.14	−4.96	–	−1.33	−0.061	0.001			−4.09	−6.88	–	−1.31	−0.075	0.004			−2.22	−4.60	–	0.17	−0.045	0.07

Abbreviations: Kyoto Scale of Psychological Development 2001(KSPD), developmental quotient (DQ), cognitive-adaptive (C-A), language-social (L-S), partial regression coefficient (B), confidence interval (CI), standardized partial regression coefficients (β), interquartile range (IQR),1 year postpartum (C-1y).

M-T1; Overall median 14.6 (IQR 11.9–17.9), Boys median 14.6 (IQR 12.0–18.1), Girls median 14.4 (IQR 11.9–17.7) pregnant weeks.

M-T2; Overall median 27.3 (IQR 25.1–30.0), Boys median 27.4 (IQR 25.3–30.3), Girls median 27.0 (IQR 25.1–29.9) pregnant weeks.

Adjusted for age of mother at the delivery, unplanned pregnancy, infertility treatment, marital status, maternal highest level of education, paternal highest level of education, maternal smoking during pregnancy, paternal smoking during pregnancy, maternal alcohol consumption during pregnancy, annual household income, maternal neuropsychiatric disorders, psychoactive drug use during pregnancy, pregnancy complications, obstetric labor complications, mode of delivery, birth weight of children, gestational week of delivery, feeding method at 6 months postpartum, family structure, number of children included subject, attendance age of daycare center, location of regional center, and sex of children for overall.

Table 5. Multiple regression analysis with stepwise method of Maternal K6 and KSPD in eight trajectories groups.

	Maternal K6			Overall ($n = 3287$)							Boys ($n = 1630$)							Girls ($n = 1657$)						
	M-T1	M-T2	C-1Y	Pr > F	R^2	*B*	95%CI			*β*	*p*	Pr > F	R^2	*B*	95%CI			*β*	*p*	Pr > F	R^2	*B*	95%CI			*β*	*p*
C-A DQ	≤4	≤4	≤4	<.0001	0.081	ref						<.0001	0.083	ref						<.0001	0.095	ref					
	≤4	≤4	≥5			−0.75	−2.77	–	1.26	−0.013	0.46			0.52	−2.37	–	3.42	0.009	0.72			−2.25	−5.04	–	0.54	−0.039	0.11
	≤4	≥5	≤4			−0.57	−2.56	–	1.42	−0.010	0.58			−0.75	−3.70	–	2.21	−0.012	0.62			−0.38	−3.08	–	2.32	−0.007	0.7
	≤4	≥5	≥5			0.45	−2.51	–	3.42	0.005	0.76			0.73	−4.12	–	5.58	0.007	0.77			−0.26	−3.95	–	3.42	−0.003	0.89
	≥5	≤4	≤4			−0.68	−2.28	–	0.93	−0.014	0.41			0.08	−2.27	–	2.43	0.002	0.95			−1.40	−3.61	–	0.80	−0.031	0.21
	≥5	≤4	≥5			−1.44	−3.92	–	1.03	−0.020	0.25			−1.57	−5.18	–	2.04	−0.021	0.39			−1.43	−4.85	–	1.99	−0.020	0.41
	≥5	≥5	≤4			−0.57	−2.33	–	1.20	−0.011	0.53			−1.24	−3.82	–	1.34	−0.024	0.34			0.07	−2.35	–	2.48	0.001	0.96
	≥5	≥5	≥5			−2.01	−3.65	–	−0.38	−0.043	0.02			−2.27	−4.71	–	0.18	−0.046	0.07			−2.00	−4.16	–	0.15	−0.046	0.07
L-S DQ	≤4	≤4	≤4	<.0001	0.104	ref						<.0001	0.087	ref						<.0001	0.136	ref					
	≤4	≤4	≥5			−1.21	−3.42	–	1.00	−0.018	0.28			−0.89	−4.11	–	2.32	−0.013	0.59			−1.63	−4.66	–	1.40	−0.025	0.29
	≤4	≥5	≤4			0.36	−1.83	–	2.55	0.005	0.75			0.15	−3.14	–	3.45	0.002	0.93			0.63	−2.30	–	3.57	0.010	0.67
	≤4	≥5	≥5			−0.22	−3.48	–	3.03	−0.002	0.89			1.04	−4.35	–	6.43	0.009	0.70			−0.65	−4.65	–	3.35	−0.008	0.75
	≥5	≤4	≤4			0.01	−1.76	–	1.78	0.000	0.99			0.45	−2.16	–	3.07	0.009	0.73			0.02	−2.37	–	2.41	0.000	0.99
	≥5	≤4	≥5			−1.33	−4.05	–	1.38	−0.016	0.34			−1.64	−5.65	–	2.38	−0.020	0.42			−0.82	−4.53	–	2.90	−0.010	0.67
	≥5	≥5	≤4			−1.40	−3.33	–	0.53	−0.025	0.15			−1.82	−4.69	–	1.05	−0.031	0.21			−0.54	−3.15	–	2.07	−0.010	0.69
	≥5	≥5	≥5			−3.27	−5.04	–	−1.50	−0.063	0.0003			−3.70	−6.41	–	−0.98	−0.068	0.008			−2.24	−4.58	–	0.10	−0.046	0.06

Abbreviations: Kyoto Scale of Psychological Development 2001(KSPD), developmental quotient (DQ), cognitive-adaptive (C-A), language-social (L-S), partial regression coefficient (B), confidence interval (CI), standardized partial regression coefficients (β), interquartile range (IQR),1 year postpartum (C-1y).

M-T1; Overall median 14.6 (IQR 11.9–17.9), Boys median 14.6 (IQR 12.0–18.1), Girls median 14.4 (IQR 11.9–17.7) pregnant weeks.

M-T2; Overall median 27.3 (IQR 25.1–30.0), Boys median 27.4 (IQR 25.3–30.3), Girls median 27.0 (IQR 25.1–29.9) pregnant weeks.

Overall; C-A DQ: Adjusted for unplanned pregnancy, marital status, maternal highest level of education, paternal highest level of education, paternal smoking during pregnancy, annual household income (×1000 yen/year) during pregnancy, maternal neuropsychiatric disorders, sex of children, birth weight of children (grams), attendance at daycare center (attendance age), Regional Center.

Overall; L-S DQ: Adjusted for maternal highest level of education, paternal highest level of education, paternal smoking during pregnancy, annual household income (×1000 yen/year) during pregnancy, pregnancy complications, sex of children, birth weigt of children (grams), feeding method at postpartum 6 months, number of children included subject, attendance at daycare center (attendance age), Regional Center.

Boys; C-A DQ: Adjusted for marital status, maternal highest level of education, paternal highest level of education, paternal smoking during pregnancy, annual household income (×1000 yen/year) during pregnancy, birth weight of children (grams), number of children included subject, Regional Center.

Boys; L-S DQ: Adjusted for age of mother at the delivery (years), maternal highest level of education, paternal highest level of education, paternal smoking during pregnancy, annual household income (×1000 yen/year) during pregnancy, birth weight of children (grams), gestation week of delivery, number of children included subject, Regional Center.

Girls; C-A DQ: Adjusted for marital status, maternal highest level of education, paternal highest level of education, paternal smoking during pregnancy, annual household income (×1000 yen/year) during pregnancy, maternal neuropsychiatric disorders, mode of delivery, birth weight of children (grams), gestation week of delivery, feeding method at postpartum 6 months, family structure, attendance at daycare center (attendance age), Regional Center.

Girls; L-S DQ: Adjusted for maternal highest level of education, paternal highest level of education, annual household income (×1000 yen/year), during pregnancy, maternal neuropsychiatric disorders, obstetric labor complications, feeding method at postpartum 6 months, number of children included subject, attendance at daycare center (attendance age), Regional Center.

M-T2 and C-1y (Table 5). There were no significant differences in the C-A DQ area (Table 5).

Overall

Multiple regression analysis without the stepwise method showed significantly low scores with maternal K6 ≥ 5 at both M-T1 and M-T2 and C-1y for the C-A DQ (*B*: −2.00, 95% CI: −3.65 – −0.35, *β*: −0.043, $p = 0.02$) and L-S DQ areas (*B*: −3.14, 95% CI: −4.96 – −1.33, *β*: −0.061, $p = 0.001$), compared to those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 4). The groups with maternal K6 scores ≤ 4 at any one or two periods during M-T1, M-T2, and C-1y were also not significantly different from those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 4).

Multiple regression analysis with the stepwise method showed significantly low scores with maternal K6 ≥ 5 at both M-T1 and M-T2 and C-1y for the C-A DQ (B: −2.01, 95% CI: −3.65 – −0.38, *β*: −0.043, $p = 0.02$) and L-S DQ areas (*B*: −3.27, 95% CI: −5.04 – −1.50, *β*: −0.063, $p = 0.0003$), compared to those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 5). The groups with maternal K6 scores ≤ 4 at any one or two periods during M-T1, M-T2, and C-1y were also not significantly different from those with maternal K6 scores ≤ 4 at both M-T1 and M-T2 and C-1y (Table 5).

Discussion

In the present study of 4-year-old children, persistent maternal psychological distress (K6 scores ≥ 5) from the first half of pregnancy to 1 year postpartum tended to be associated with lower verbal cognitive development in boys, but not in girls. In contrast, in the group without persistent maternal psychological distress from the first half of pregnancy to 1 year postpartum, no significant impact was observed on verbal cognitive development, regardless of the children's sex.

Sex-specific differences

Our study showed that maternal perinatal psychological distress tended to lead to lower verbal cognitive development in boys, but not in girls, at 4 years of age. At present, the reasons and mechanisms behind this phenomenon remain unknown, and further research is warranted. It is worth noting that although not specific to verbal cognitive development, several studies have found sex-specific effects, suggesting that boys are more vulnerable to maternal perinatal stress than girls.[1,2,5] King *et al.* reported a linear decline in IQ with increasing maternal prenatal objective stress exposure among boys. However, no such effect was observed among girls aged 11 years.[19] Simcock *et al.* reported that higher levels of objective flood exposure predicted a more irritable temperament in boys, but not girls, at the age of 6 months.[20] Gerardin *et al.* reported that infants of mothers with prenatal depression presented higher scores on generalized anxiety, activity/impulsivity, and sleep problems than controls, particularly boys aged 1 year.[21] Loomans *et al.* reported that prenatal maternal anxiety was associated with hyperactivity/inattention in boys aged 5 years.[22] Li *et al.* reported that prenatal maternal exposure to severe stress increases the risk of attention-deficit/hyperactivity disorder (ADHD) in boys.[23] Zhu *et al.* also reported that in mothers who experienced severe stressful prenatal life events, there was an increased risk for ADHD in boys, but not in girls.[24] Fineberg *et al.* reported that maternal daily-life stress during pregnancy was associated with significantly increased odds of schizophrenia spectrum disorders in boys.[25] Glasheen *et al.* reported that maternal prenatal and postnatal anxiety was associated with a higher risk of conduct disorder among boys; however, it was less likely in girls aged 16 years.[26]

Others have found girls to be more vulnerable, particularly to emotional problems. Buss *et al.* reported that higher maternal cortisol levels during early gestation were associated with more affective problems in girls aged 7.5 years.[27] Braithwaite *et al.* reported that girls exposed to high levels of maternal prenatal cortisol were more emotionally negative than boys at 2 months of age.[28,29] Wright *et al.* reported that an elevated maternal prenatal cortisol level was associated with lower callous-unemotional traits in girls, but not in boys, at 2.5–5.0 years of age.[30] As this study was based solely on K6 points based on the questionnaire and did not examine cortisol levels, future studies are needed to determine how the effects of K6 trajectories and cortisol levels on children differ by sex.

Sex differences have been observed in rodents. For example, Weinstock found that male rats subjected to prenatal stress had greater learning deficits than did female rats, with greater long-term hippocampal potentiation, hippocampal neurogenesis, and reduced dendritic spine density in the prefrontal cortex.[31–33] These sex differences may be due to the developing brain regions' sensitivity to stress hormones. Decreased testosterone and aromatase activity combined with the effects of other corticosteroids may contribute to learning deficits in male rats.[34] In contrast, estrogen has protective effects on brain regions associated with learning and memory in rats and mice.[35–37]

Clinical periods vulnerable to the effect of maternal psychological distress trajectories

Our study examined maternal psychological distress during three periods: the first half of pregnancy at approximately 14 weeks, the second half of pregnancy at approximately 27 weeks, and 1 year postpartum. We observed that persistent maternal psychological distress from the first half of pregnancy to 1 year postpartum had a negative association with verbal cognitive development in boys. Even overall, persistent maternal psychological distress from the first half of pregnancy to 1 year postpartum had a disadvantageous association with verbal and nonverbal cognitive development. No such association was noted in mothers who were not psychologically distressed (K6 scores ≤ 4) at any one or two of these three periods.

In a similar study that focused specifically on children's cognitive development, Lin *et al.* reported that children's cognitive development may be more susceptible to prenatal exposure to maternal emotional stress than postnatal emotional stress, at the age of 24–30 months.[38]

Although not specific to cognitive development, several studies have reported clinical periods associated with children's vulnerability to the effects of maternal psychological distress trajectories on their neurodevelopment. Van der Waerden *et al.* reported that children whose mothers had persistent depressive symptoms, either intermediate or severe, from pregnancy to the postpartum period, had the greatest emotional and behavioral difficulties at the age of 5 years.[39] Fransson *et al.* reported that maternal prenatal and postpartum depression is associated with more behavioral problems in children. Girls are affected to a greater degree at 18 months of age.[40] Lin *et al.* reported that children's temperamental development may be more susceptible to postnatal exposure to

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maternal emotional stress than to prenatal exposure, at the age of 24–30 months.[38]

For reference, although the research design blended prenatal and postpartum periods, Srinivasan *et al.* reported that children of mothers who experience depression in the perinatal period are more likely to report psychotic experiences at 18 years of age.[41] Oh *et al.* also reported that maternal perinatal depression up to 2 years postpartum affects childhood behavioral problems and executive function at 9 years of age.[42]

Clinical implications

Undoubtedly, prenatal and postpartum maternal depression, anxiety, and stress negatively affect neurodevelopment, including cognitive performance, in children.

In our previous study using JECS data, persistent maternal psychological distress from the first to the second half of pregnancy was a risk factor for autism spectrum disorder among children.[14] Our current study also suggests that persistent maternal psychological distress from the first half of pregnancy to the first year postpartum had a negative effect on boys' verbal cognitive development at 4 years of age. In light of this finding, assessing the mental health of pregnant women during the early stages of pregnancy is essential. For women who experience psychological distress during early pregnancy, appropriate interventions to prevent continued psychological distress throughout the pregnancy and at least in the postpartum period are important.

Limitations

This study has several limitations. First, K6 is a self-administered questionnaire; therefore, the mothers' psychological distress was not medically diagnosed. However, this questionnaire can be used because previous studies have shown reasonable results with it.[12,13] Second, the Sub-Cohort Study was based on 5,000 participants (5%) who were selected from the total births. In reality, 3,287 participants (3.3%) were analyzed in this study. There may be an intrinsic bias in the sub-sample used for the study.

Strengths of the study

This was a large prospective birth cohort study in which certified testers objectively assessed the cognitive development of 3,287 children at 4 years of age.

Conclusion

Persistent maternal psychological distress from the first half of pregnancy to 1 year postpartum had a disadvantageous association with verbal cognitive development in boys, but not in girls, at 4 years of age. The JECS is a prospective study that plans to follow and evaluate the development of the targeted children until they reach 40 years of age. In the future, we plan to further evaluate children's neurodevelopment, including changes in the effects of maternal prenatal and postnatal psychological distress on children's development.

Data availability statement. Data are unsuitable for public deposition due to ethical restrictions and the legal framework of Japan. It is prohibited by the Act on the Protection of Personal Information (Act No.57 of 30 May 2003, amendment on 9 September 2015) to publicly deposit data containing personal information. Ethical Guidelines for Epidemiological Research enforced by the Japan Ministry of Education, Culture, Sports, Science and Technology and the Ministry of Health, Labour and Welfare also restricts the open sharing of epidemiologic data. All inquiries regarding access to data should be sent to: pj.o g.sein@ne-scej. The person responsible for handling enquiries sent to this email address is Dr Shoji F. Nakayama, JECS Programme Office, National Institute for Environmental Studies.

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Ethical standards. The authors assert that all procedures contributing to this work comply with the ethical standards of the Ministry of the Environment's Institutional Review Board on Epidemiological Studies (no. 100910001) and with the Helsinki Declaration of 1975, as revised in 2008, and have been approved by the institutional committees of all participating institutions. Written informed consent was obtained from all participants.

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