

Original Article

Maternal fermented food intake and infant neurodevelopment: The Japan Environment and Children's Study

Tomomi Tanaka MD, PhD^{1,2}, Kenta Matsumura PhD^{2,3}, Akiko Tsuchida PhD^{2,3}, Kei Hamazaki MD, PhD^{3,4}, Haruka Kasamatsu MEd², Hiroko Hirai MD¹, Shohei Kusabiraki MD¹, Akiko Hiraiwa MD, PhD¹, Kazushi Miya MD, PhD^{1,5}, Yuichi Adachi MD, PhD¹, Hidekuni Inadera MD, PhD^{2,3}, and The Japan Environment and Children's Study (JECS) Group

¹Department of Pediatrics, Faculty of Medicine, University of Toyama, Toyama, Toyama, Japan

²Toyama Regional Center for JECS, University of Toyama, Toyama, Toyama, Japan

³Department of Public Health, Faculty of Medicine, University of Toyama, Toyama, Toyama, Japan

⁴Department of Public Health, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan

⁵School of Education, University of Toyama, Toyama, Toyama, Japan

Background and Objectives: Fermented foods play an important role in establishing intestinal bacterial flora, and the composition of the intestinal bacterial flora might be associated with neurodevelopment. This study investigated the association between maternal intake of fermented foods during pregnancy and early neurodevelopment in offspring. **Methods and Study Design:** Data were analyzed for 73,522 pregnant women participating in the Japan Environment and Children's Study. Their intake of four common fermented foods during pregnancy was assessed using a semi-quantitative FFQ. Neurodevelopment in their infants at 1 year of age was estimated using the Ages and Stages Questionnaires. **Results:** Multivariable logistic regression analysis showed that maternal intake of miso soup and fermented soybeans was each associated with a significantly reduced risk of delay in infant communication skills. Maternal intake of fermented soybeans and cheese was each associated with a significantly reduced risk of delay in fine motor skills in the third and fourth quartiles. For problem-solving, preventive associations were observed with maternal intake of fermented soybeans in the second and third quartiles and with maternal intake of cheese in the third and fourth quartiles. Maternal intake of yogurt was associated with a significantly reduced risk of delay in personal-social skills in the third and fourth quartiles, while that of cheese was associated with a reduced risk in the third quartile. No reductions in risk were observed for gross motor skills. **Conclusions:** Our results suggest that fermented food intake during pregnancy may have beneficial associations with several areas of psychomotor development in children.

Key Words: fermented foods, soy foods, yogurt, cheese, child development

INTRODUCTION

Bacterial fermentation makes foods suitable for long-term storage and changes their nutritional value and taste. A considerable variety of fermented foods exist, and many such as miso, fermented soybeans, and pickled vegetables are an integral part of the regular Japanese diet.

It is now recognized that the consumption of fermented foods can prevent the development of various diseases, including diabetes mellitus,¹ allergy,² depression,³ obesity,⁴ atopic dermatitis,⁵ constipation,⁶ and irritable bowel syndrome.⁷ Moreover, diet can influence the composition of the intestinal bacterial flora. Fermented foods in particular play an important role in the formation of the intestinal bacterial flora in humans. For example, Mikami et al.⁸ identified the influence of maternal intestinal and vaginal bifidobacteria on the establishment of bifidobacteria colonization in the neonatal gut.

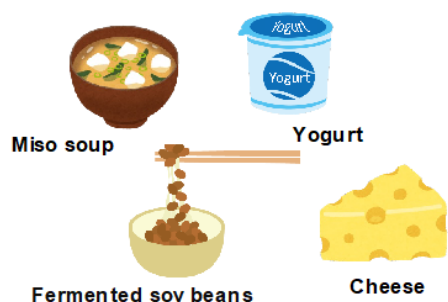
Recently, the participation of the gut-brain axis in the pathogenesis of various kinds of diseases has attracted considerable attention, and accumulating evidence suggests that changes in the composition of intestinal bacterial flora play an important role in the gut-brain axis.⁹ Other work has shown that there is a relationship between autism spectrum disorder (ASD) and intestinal bacterial flora.¹⁰⁻¹² Therefore, we speculated that the composition

Corresponding Author: Dr Tomomi Tanaka, Department of Pediatrics, Faculty of Medicine, University of Toyama, 2630 Sugitani, Toyama City, Toyama 930-0194, Japan
Tel: +81-76-434-7313; Fax: +81-76-434-5029
Email: tharai@med.u-toyama.ac.jp

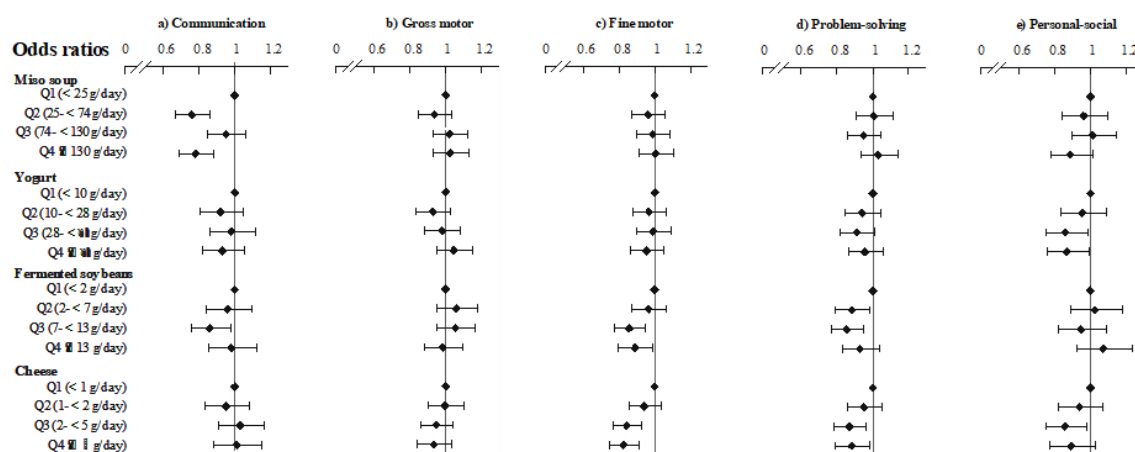
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Japan Environment and Children's Study

Exposures



Outcomes



Graphical abstract

of intestinal bacterial flora may be associated with not only neurological diseases but also with neurodevelopment in children. Few studies using large-scale cohorts have evaluated the relationship between maternal intake of fermented foods during pregnancy and early neurodevelopment in offspring. We hypothesized that fermented food intake during pregnancy would prevent neurodevelopmental delay in offspring.

In this study, we analyzed a dataset for approximately 100,000 pregnant Japanese women obtained from the Japan Environment and Children's Study (JECS) to investigate associations between maternal intake of four fermented foods commonly consumed during pregnancy and early neurodevelopment in infants at 1 year of age.

METHODS

Study population

The JECS is a nationwide government-funded birth cohort study investigating the links between environmental factors and children's health and development. The pregnant women participating in the JECS were recruited from 15 areas across Japan between January 2011 and March 2014. The methods of the JECS have been described in detail elsewhere.^{13,14}

The present study was based on the jecs-an-20180131 dataset that was released in March 2018. The full dataset includes 103,062 pregnancies, from which 5,647 were excluded because of multiple participations, 949 were excluded because of multiple births, and 3,676 were ex-

cluded because of miscarriages or stillbirths (Figure 1). We also excluded 19,268 records from the analysis because of missing information on maternal diet and/or infant developmental delay. This left data for 73,522 mother–infant pairs for analysis in this study. All data were obtained from self-reported questionnaires and drug interviews, including information on the maternal intake of fermented foods.

Ethics approval and consent to participate

The JECS comprehensive protocol was reviewed and approved by the Ministry of the Environment's Institutional Review Board on Epidemiological Studies (100910001) and the ethics committees of all participating institutions. This specific study was approved by the Ethics Committee of the University of Toyama (R2018032). JECS is conducted in accordance with the Helsinki Declaration and other national regulations, and written informed consent was obtained from parents/guardians of participants who were under 16 years of age.

Fermented foods

Maternal intake of four fermented foods—miso soup, fermented soybeans, yogurt, and cheese—in the average diet from the beginning of pregnancy was assessed using a semi-quantitative FFQ during the second or third trimester. The questionnaire comprised a list of foods with standard portion sizes commonly consumed in Japan.¹⁵

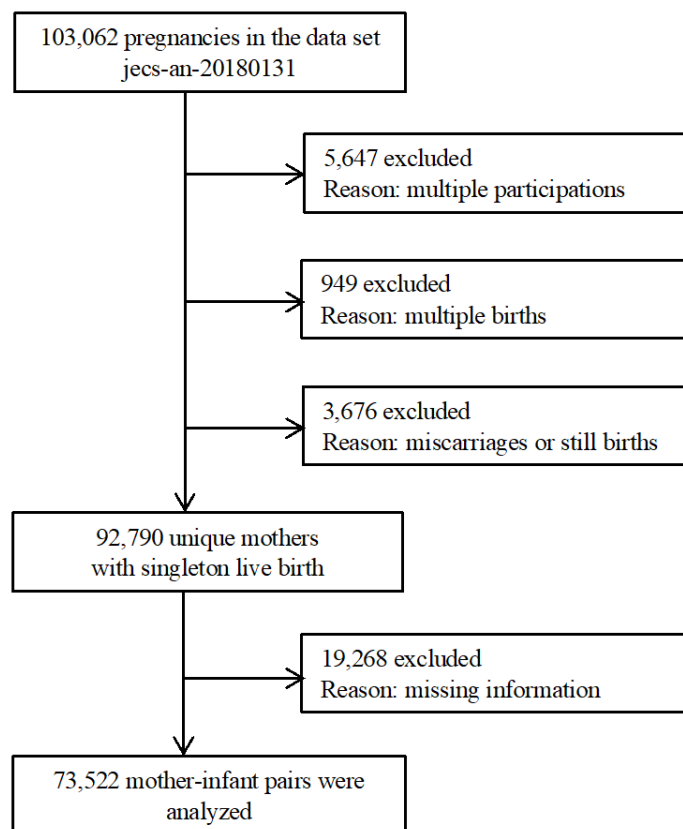


Figure 1. Flow diagram of the recruitment and exclusion process for the participants. The full dataset included 103,062 pregnancies, with 5,647, 949, and 3,676 pregnancies excluded because of multiple participations, multiple births, and miscarriages or stillbirths, respectively. We also excluded data for 19,268 records because of missing information. Finally, 73,522 individuals were analyzed in this study.

The intake amount of each food was categorized according to the quartile for each of the four fermented food groups.¹⁶

Neurodevelopment

The primary outcome of this study was early neurodevelopment in offspring at 1 year of age. Neurodevelopment was evaluated with the Ages and Stages Questionnaires (ASQ-3): A Parent-Completed Child Monitoring System, which is a validated scale that has been recommended by UNICEF to verify whether children have normal neurological development.¹⁷ The Japanese version of the ASQ-3 has been validated¹⁸ and used in several studies.¹⁹ The scale comprises 21 age-specific structured questionnaires across five domains: communication, gross motor skills, fine motor skills, problem-solving skills, and personal-social skills.²⁰ The questionnaire comprises 30 questions (5 per domain) that can be answered with “yes,” “sometimes,” or “not yet.” “Yes,” which corresponds to 10 points, indicates that the respondent’s child demonstrates the ability to do the specific activity described by the item; “sometimes,” which corresponds to 5 points, indicates that the skill of the respondent’s child is emerging; and “not yet,” which corresponds to 0 points, indicates that the respondent’s child has not yet shown evidence of the ability to do that specific activity. Scores range from 0 to 60 for each domain.²⁰ If one or two answers to the six questions were missing, a correction coefficient of 1.2 or 1.5, respectively, was multiplied by the remaining total score to adjust the score to be between 0 and 60. If more

than three of the six questions were not answered, then the participant was excluded from the analysis.

To evaluate the neurodevelopmental status of children at 1 year of age, we included participants who responded to the ASQ-3 when their child was 10–13 months old. For premature infants born before 37 weeks of gestation, their corrected age was used. Two items addressed behaviors that children may have exhibited previously but no longer did because they had acquired more advanced skills (one in the fine motor domain and another in the problem-solving domain). If parents answered “not yet” or “sometimes” to an easier item but “yes” to a more advanced item, responses for the earlier items were changed to “yes.” In this study, neurodevelopmental delay was defined as a score <2 standard deviations from the mean for each development domain of each question.

Statistical analysis

Data are expressed as the mean \pm standard deviation or median, unless stated otherwise. To estimate the risk of neurodevelopmental delay for each level of the fermented foods consumed, we categorized the participants into four groups according to the intake amount of each fermented food. Then, we performed logistic regression analysis to calculate the ORs and 95% CIs.

We included potential confounding factors and covariates in the statistical analysis if they had been (or are theoretically inferred to be) associated with the outcome in previous studies. The confounding factors and covariates used in the present study were as follows: maternal age; previous deliveries (nulliparous or multiparous); energy

intake; folic acid intake; physical activity; intake of anti-bacterial drugs; marital status (married [including common-law status], single [never married], divorced, or widowed); pre-pregnancy BMI (kg/m², categorized as <18.5, 18.5 to <25, or ≥25); alcohol intake (never, quit before learning of current pregnancy, quit after learning of the pregnancy, or currently drinking); active smoking status (never smoked, quit before learning of current pregnancy, quit after learning of current pregnancy, currently smoking ≤10 cigarettes, or currently smoking >10 cigarettes); passive smoking status (no one in the household smoked, somebody smoked but not in the presence of the baby, or somebody smoked in the presence of the baby); annual household income (<4 million, 4–6 million, or >6 million JPY); highest maternal educational level (junior high or high school; technical junior college, technical/vocational college, or associate degree; Bachelor's degree or postgraduate degree); employment status (yes or no); offspring's sex (male or female); period of gestation; mode of delivery (vaginal delivery or cesarean section); birth weight; presence of any congenital anomaly (yes or no); and highest educational level of partner. The variables were categorized according to standard medical practice, common practice in Japan, and/or based on previous studies.²¹

Two-sided *p*-values <0.05 were considered statistically significant. Data were analyzed using SAS version 9.4 software (SAS Institute Inc., Cary, NC).

RESULTS

Participant characteristics

Table 1 shows the total demographic and obstetric characteristics of the participants in this study, and maternal characteristics according to the quartile for each fermented food are shown in Supplementary Tables 1–4. Compared with mothers who reported low miso soup consumption, those who reported higher miso soup consumption were approximately 10% more likely to be multiparous (Supplementary Table 1). Compared with mothers who reported low yogurt consumption, those who reported higher yogurt consumption had a higher level of education and annual household income, were more likely not to smoke or be exposed to passive smoke, were more likely to be nulliparous, and had a partner with a higher level of education (Supplementary Table 3). Compared with mothers who reported low cheese consumption, those who reported higher cheese consumption had a higher level of education, were more likely not to be exposed to passive smoke, and had a partner with a higher level of education (Supplementary Table 4). For all fermented foods, women who reported higher consumption had a higher energy intake than those who reported low consumption (Supplementary Tables 1–4).

Multivariable logistic regression of neurodevelopmental delay in offspring

Figure 2 shows forest plots of adjusted ORs and 95% CIs for cases of developmental delay in each area—communication, gross motor, fine motor, problem-solving, personal-social skills—assessed using the ASQ-3 according to the exposure variable. For more information, Supplementary Tables 5–9 show multivariable ORs for

the relationships between maternal consumption of fermented foods and early neurodevelopmental status in offspring for each of the five domains.

Maternal intake of miso soup was associated with a significantly reduced risk of delay in communication skills in the second and fourth quartiles, and maternal intake of fermented soybeans was associated with a reduced risk in the third quartile (Supplementary Table 5). Maternal intake of fermented soybeans was associated with a significantly reduced risk of delay in fine motor development in the third and fourth quartiles, and maternal intake of cheese showed associated preventive effects in the third and fourth quartiles (Supplementary Table 7). For problem-solving, associated preventive effects were observed with maternal intake of fermented soybeans in the second and third quartiles, and with maternal intake of cheese in the third and fourth quartiles (Supplementary Table 8). Supplementary Table 9 shows that maternal intake of yogurt was associated with a significantly reduced risk of delay in personal-social skills in the third and fourth quartiles and that of cheese was associated with a reduced risk in the third quartile. No reductions in risk were observed for gross motor skills (Supplementary Table 6).

DISCUSSION

In this study, we found that maternal intake of fermented foods during pregnancy may protect against neurodevelopmental delay in early childhood, supporting our initial hypothesis. Among the five neurodevelopmental domains assessed, the effects were clearly observed in communication, fine motor, problem-solving, and personal-social skills.

The gut–brain axis is a dynamic bidirectional neuroendocrine system used to describe the connections between the gastrointestinal tract and nervous system. Three basic pathways mediating communication between the gut and brain have been proposed: direct neuronal communication, endocrine signaling mediators, and the immune system.²² There are many regulatory factors that are common to the enteric and central nervous systems. Both hormones secreted by intestinal enterochromaffin cells and metabolites produced by the gut microbiota interact with biochemical pathways that influence central nervous system processes by creating a means of direct communication between the external environment and brain.

In the context of the gut–brain axis, associations have been found between bacterial intestinal flora and developmental disorders in children. Nikolov et al.¹¹ reported that 39 of 172 children (22.7%) with pervasive developmental disorders were positive for gastrointestinal problems, primarily constipation and diarrhea. Furthermore, compared with children without gastrointestinal problems, those with them showed greater symptom severity in measures of irritability, anxiety, and social withdrawal. De Angelis et al.¹⁰ evaluated the fecal microbiota in patients with ASD and pervasive developmental disorder not otherwise specified and in healthy children and found that levels of *Clostridium* and *Bacteroides* genera were higher in children with ASD and that levels of *Bifidobacterium* species were lower in children with ASD compared with healthy children. These findings suggest that

Table 1. Demographic and obstetric characteristics of the participants (n = 73,522)

	Mean/N	(SD/%)
Maternal age, mean (SD)	31.1	(5.0)
Previous deliveries		
Nulliparous	31,529	(44.0)
Multiparous	40,125	(56.0)
Energy intake (kcal), mean (SD)	1,728	(763.6)
Folic acid (mg), mean (SD)	0.3	(0.2)
Physical activity (MET·h/day), mean (SD)	3.9	(8.2)
Antibacterial drug intake		
No	65,658	(89.3)
Yes	7,864	(10.7)
Marital status		
Married (including common-law marriage)	69,903	(95.8)
Single (never married)	2,529	(3.5)
Divorced or widowed	538	(0.7)
Pre-pregnancy BMI (kg/m ²)		
<18.5	11,907	(16.2)
18.5 to <25	54,351	(74.0)
≥25	7,225	(9.8)
Alcohol intake		
Never	24,507	(33.6)
Quit before learning of pregnancy	11,942	(16.4)
Quit after learning of pregnancy	34,576	(47.4)
Currently drinking	1,986	(2.7)
Active smoking status		
Never	43,894	(60.1)
Quit before learning of pregnancy	16,476	(22.5)
Quit after learning of pregnancy	10,151	(13.9)
Currently smoking 10 cigarettes or less	2,050	(2.8)
Currently smoking more than 10 cigarettes	501	(0.7)
Passive smoking status		
No one in the household smoked	35,722	(48.8)
Somebody smoked but not in the presence of the baby	35,804	(48.9)
Somebody smoked in the presence of the baby	1,634	(2.2)
Annual household income (JPY)		
<4 million	26,872	(39.2)
4–6 million	22,932	(33.4)
>6 million	18,806	(27.4)
Highest educational level		
Junior high or high school	25,204	(34.4)
Technical junior college, technical/vocational college, or associate degree	31,226	(42.7)
Bachelor's degree or postgraduate degree	16,749	(22.9)
Highest educational level of partner		
Junior high or high school	31,002	(42.6)
Technical junior college, technical/vocational college, or associate degree	16,565	(22.8)
Bachelor's degree or postgraduate degree	25,205	(34.6)
Employed		
No	33,252	(45.6)
Yes	39,694	(54.4)

SD, standard deviation; MET, metabolic equivalents; JPY, Japanese yen.

the intestinal bacterial flora may promote the main symptoms and deuteropathies in patients with ASD.

Fermented foods improve intestinal bacterial flora, and their effect is produced mainly by probiotics, including *Bifidobacterium*, *Lactobacillus*, and *Streptococcus* species. Furthermore, functional components produced by the fermentation process affect intestinal flora. The colonization of the intestinal bacterial flora begins immediately at birth, and the original bacterial community is established within the first week after birth.²³ Furthermore, the

formation of the intestinal bacterial flora during the neonatal period will dictate immune system development in childhood and affect the composition of the intestinal bacterial flora for the child's entire life. In addition, one of the most important determinants of intestinal bifidobacteria in infants is the colonization of *Bifidobacterium breve* in the mother's gut and vagina.⁸ Interestingly, Aagaard et al.²⁴ reported a unique placental microbiome niche comprising nonpathogenic commensal microbiota from the Firmicutes, Tenericutes, Proteobacteria,

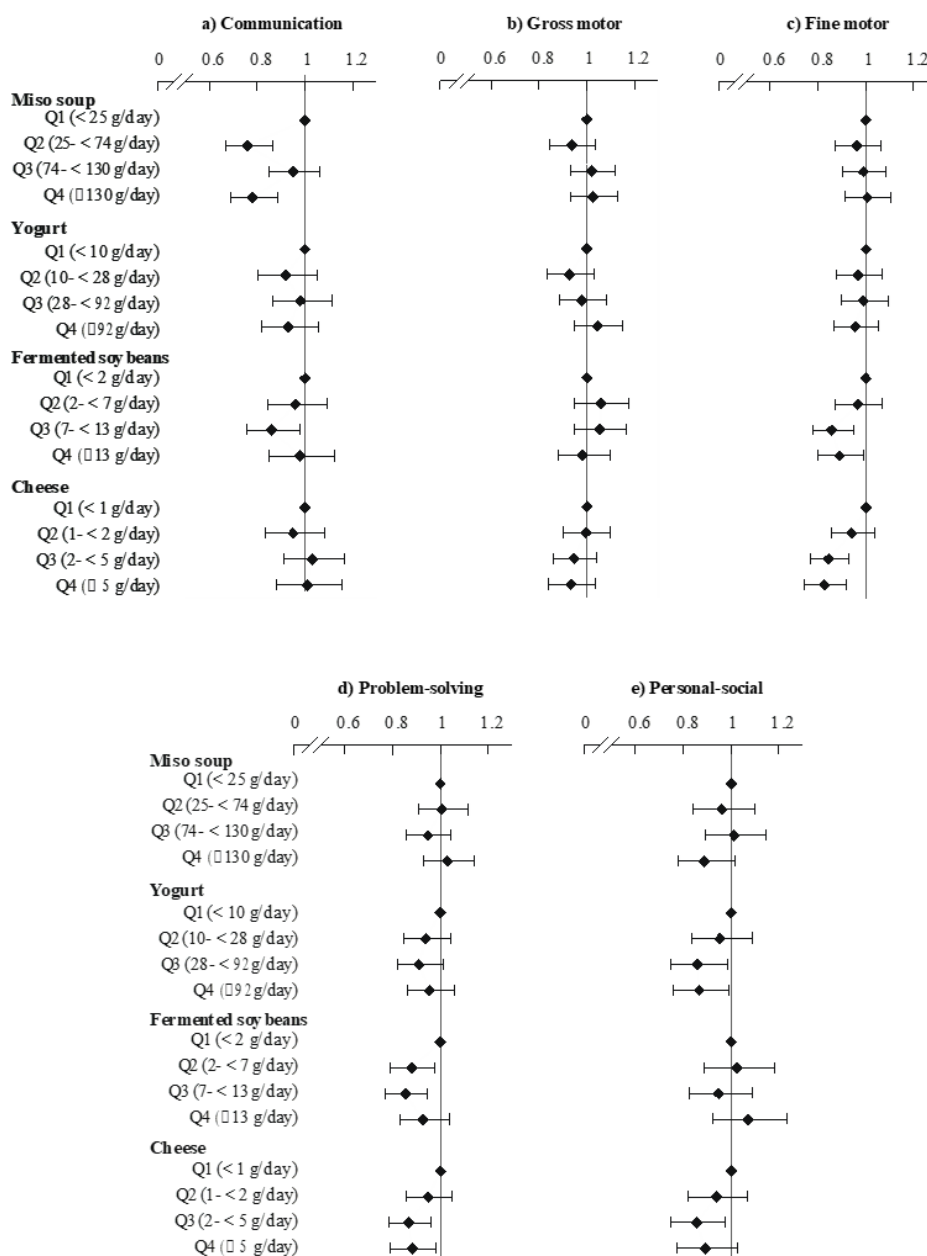


Figure 2. Forest plots of developmental delay. Forest plots of adjusted ORs and 95% CIs for the cases of developmental delay in each area assessed using the ASQ-3 according to the exposure variable. Q1, first quartile; Q2, second quartile; Q3, third quartile; Q4, fourth quartile.

†Adjusted for maternal age, previous deliveries, energy intake, folic acid intake, physical activity, intake of antibacterial drugs, marital status, pre-pregnancy BMI, alcohol intake, active smoking status, passive smoking status, annual household income, highest maternal educational level, offspring’s sex, period of gestation, mode of delivery, birth weight, presence of any congenital anomaly and highest educational level of partner.

Bacteroidetes, and *Fusobacteria phyla*. Thus, the maternal intake of fermented foods during pregnancy may affect the fetus from a relatively early stage.

Notably, communication impairments and developmental delay in fine motor and personal-social skills, which were identified in the present study, are well-known features of children with ASD. ASD involves complex neurodevelopmental dysfunctions that are characterized by impairments in social interaction and communication, as well as by restricted patterns of interest and repetitive behaviors.¹⁰ In this study, we used the ASQ-3 to estimate the early developmental status. However, it is difficult to determine whether the results of this study estimate symptoms of ASD or the characteristics of

children who are not categorized as having ASD. Therefore, long-term follow-up is needed for those children suspected of having neurodevelopmental delay in this study.

Moreover, the maternal intake of fermented foods did not affect children’s gross motor skills in this study. This finding may indicate that the maternal intake of fermented foods affects only neurodevelopment, not motor development, although the mechanisms are unclear.

There are some limitations to our study. First, we did not evaluate the composition of the mothers’ or infants’ intestinal bacterial flora, which may be affected by other factors, including other dietary habits, infections (such as gastroenteritis), and the use of antibacterial drugs. Sec-

ond, neurodevelopmental status was evaluated only at 1 year of age. Some children may exhibit developmental delay gradually after this age, while others who have neurodevelopmental delay during early infancy often catch up later. Additionally, it is difficult to judge whether a child has a developmental disorder such as ASD and attention-deficit/hyperactivity disorder at 1 year of age. Thus, similar studies should be conducted later in development to investigate this topic further. Third, because this study used a self-reported questionnaire, it is unclear whether the answers of the questionnaire correctly reflected mothers' food consumption and the developmental status of their children.

In conclusion, we found an association between the maternal intake of fermented foods during pregnancy and early neurodevelopment in offspring, suggesting that if pregnant women were to consume more fermented foods, their children might avoid neurodevelopmental delay in early childhood. We plan to conduct a follow-up study when these children are 3 years old to further clarify the association further.

DATA AVAILABILITY

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 Medical and Health Research Involving Human Subjects 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 the epidemiologic data. All inquiries about access to data should be sent to: jecsen@nies.go.jp. The person responsible for handling enquiries sent to this e-mail address is Dr. Shoji F. Nakayama, JECS Programme Office, National Institute for Environmental Studies.

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Members of the JECS Group as of 2022: Michihiro Kamijima (Principal Investigator, Nagoya City University, Nagoya, Japan), Shin Yamazaki (National Institute for Environmental Studies, Tsukuba, Japan), Yukihiro Ohya (National Center for Child Health and Development, Tokyo, Japan), Reiko Kishi (Hokkaido University, Sapporo, Japan), Nobuo Yaegashi (Tohoku University, Sendai, Japan), Koichi Hashimoto (Fukushima Medical University, Fukushima, Japan), Chisato Mori (Chiba University, Chiba, Japan), Shuichi Ito (Yokohama City University, Yokohama, Japan), Zentarō Yamagata (University of Yamanashi, Chuo, Japan), Hidekuni Inadera (University of Toyama, Toyama, Japan), Takeo Nakayama (Kyoto University, Kyoto, Japan), Tomotaka Sobue (Osaka University, Suita, Japan), Masayuki Shima (Hyogo Medical University, Nishinomiya, Japan), Hiroshige Nakamura (Tottori University, Yonago, Japan), Narufumi Suganuma (Kochi University, Nankoku, Japan), Koichi Kusuhara (University of Occupational and Environmental Health, Kitakyushu, Japan), and Takahiko Katoh (Kumamoto University, Kumamoto, Japan)

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare that they have no competing interests.

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REFERENCES

- Li W, Ruan W, Peng Y, Wang D. Soy and the risk of type 2 diabetes mellitus: A systematic review and meta-analysis of observational studies. *Diabetes Res Clin Pract.* 2018;137:190-9. doi: 10.1016/j.diabres.2018.01.010.
- Ishida Y, Nakamura F, Kanzato H, Sawada D, Yamamoto N, Kagata H, Oh-Ida M, Takeuchi H, Fujiwara S. Effect of milk fermented with *Lactobacillus acidophilus* strain L-92 on symptoms of Japanese cedar pollen allergy: a randomized placebo-controlled trial. *Biosci Biotechnol Biochem.* 2005;69:1652-60. doi: 10.1271/bbb.69.1652.
- Vlainić JV, Šuran J, Vlainić T, Vukorep AL. Probiotics as an adjuvant therapy in major depressive disorder. *Curr Neuropharmacol.* 2016;14:952-8. doi: 10.2174/1570159x14666160526120928.
- Nagata S, Chiba Y, Wang C, Yamashiro Y. The effects of the *Lactobacillus casei* strain on obesity in children: a pilot study. *Benef Microbes.* 2017;8:535-43. doi: 10.3920/bm2016.0170.
- Torii S, Torii A, Itoh K, Urisu A, Terada A, Fujisawa T, et al. Effects of oral administration of *Lactobacillus acidophilus* L-92 on the symptoms and serum markers of atopic dermatitis in children. *Int Arch Allergy Immunol.* 2011;154:236-45. doi: 10.1159/000321110.
- Wojtyniak K, Horvath A, Dziechciarz P, Szajewska H. *Lactobacillus casei rhamnosus* Lcr35 in the management of functional constipation in children: a randomized trial. *J Pediatr.* 2017;184:101-5.e101. doi: 10.1016/j.jpeds.2017.01.068.
- Sandhu BK, Paul SP. Irritable bowel syndrome in children: pathogenesis, diagnosis and evidence-based treatment. *World J Gastroenterol.* 2014;20:6013-23. doi: 10.3748/wjg.v20.i20.6013.
- Mikami K, Takahashi H, Kimura M, Isozaki M, Izuchi K, Shibata R, Sudo N, Matsumoto H, Koga Y. Influence of maternal bifidobacteria on the establishment of bifidobacteria colonizing the gut in infants. *Pediatr Res.* 2009;65:669-74. doi: 10.1203/PDR.0b013e31819ed7a8.
- Cryan JF, Dinan TG. Mind-altering microorganisms: the impact of the gut microbiota on brain and behaviour. *Nat Rev Neurosci.* 2012;13:701-12. doi: 10.1038/nrn3346.
- De Angelis M, Piccolo M, Vannini L, Siragusa S, De Giacomo A, Serrazanetti DI, Cristofori F, Guerzoni ME, Gobbetti M, Francavilla R. Fecal microbiota and metabolome of children with autism and pervasive developmental disorder not otherwise specified. *PLoS One.* 2013;8:e76993. doi: 10.1371/journal.pone.0076993.
- Nikolov RN, Bearss KE, Lettinga J, Erickson C, Rodowski M, Aman MG, et al. Gastrointestinal symptoms in a sample of children with pervasive developmental disorders. *J Autism Dev Disord.* 2009;39:405-13. doi: 10.1007/s10803-008-0637-8.
- Santocchi E, Guiducci L, Fulceri F, Billeci L, Buzzigoli E, Apicella F, Calderoni S, Grossi E, Morales MA, Muratori F. Gut to brain interaction in Autism Spectrum Disorders: a randomized controlled trial on the role of probiotics on clinical, biochemical and neurophysiological parameters. *BMC Psychiatry.* 2016;16:183. doi: 10.1186/s12888-016-0887-5.
- Kawamoto T, Nitta H, Murata K, Toda E, Tsukamoto N, Hasegawa M, et al. Rationale and study design of the Japan Environment and Children's Study (JECS). *BMC Public Health.* 2014;14:25. doi: 10.1186/1471-2458-14-25.

14. Michikawa T, Nitta H, Nakayama SF, Yamazaki S, Isobe T, Tamura K, et al. Baseline profile of participants in the Japan Environment and Children's Study (JECS). *J Epidemiol.* 2018;28:99-104. doi: 10.2188/jea.JE20170018.
15. Yokoyama Y, Takachi R, Ishihara J, Ishii Y, Sasazuki S, Sawada N, et al. Validity of short and long self-administered food frequency questionnaires in ranking dietary intake in middle-aged and elderly Japanese in the Japan Public Health Center-Based Prospective Study for the Next Generation (JPHC-NEXT) protocol area. *J Epidemiol.* 2016;26:420-32. doi: 10.2188/jea.JE20150064.
16. Sugimori N, Hamazaki K, Matsumura K, Kasamatsu H, Tsuchida A, Inadera H, JECS Group. Association between maternal fermented food consumption and infant sleep duration: The Japan Environment and Children's Study. *PLoS One.* 2019;14:e0222792. doi: 10.1371/journal.pone.0222792.
17. Romero Otalvaro AM, Granana N, Gaeto N, Torres MLA, Zamblera MN, Vasconez MA, Misenta C, Rouvier ME, Squires J. ASQ-3: validation of the Ages and Stages Questionnaire for the detection of neurodevelopmental disorders in Argentine children. *Arch Argent Pediatr.* 2018;116:7-13. doi: 10.5546/aap.2018.eng.7.
18. Mezawa H, Aoki S, Nakayama SF, Nitta H, Ikeda N, Kato K, et al. Psychometric profile of the Ages and Stages Questionnaires, Japanese translation. *Pediatr Int.* 2019;61:1086-95. doi: 10.1111/ped.13990.
19. Matsumura K, Hamazaki K, Tsuchida A, Inadera H, JECS Group. House dust avoidance during pregnancy and subsequent infant development: The Japan Environment and Children's Study. *Int J Environ Res Public Health.* 2021;18:4277. doi: 10.3390/ijerph18084277.
20. Squires J. ASQ-3 user's guide. Baltimore: Paul H. Brookes Pub.; 2009.
21. Matsumura K, Hamazaki K, Tsuchida A, Inadera H, JECS Group. Male intake of omega-3 fatty acids and risk of intimate partner violence perpetration: a nationwide birth cohort - the Japan Environment and Children's Study. *Epidemiol Psychiatr Sci.* 2022;31:e45. doi: 10.1017/S2045796022000294.
22. Westfall S, Lomis N, Kahouli I, Dia SY, Singh SP, Prakash S. Microbiome, probiotics and neurodegenerative diseases: deciphering the gut brain axis. *Cell Mol Life Sci.* 2017;74:3769-87. doi: 10.1007/s00018-017-2550-9.
23. Mackie RI, Sghir A, Gaskins HR. Developmental microbial ecology of the neonatal gastrointestinal tract. *Am J Clin Nutr.* 1999;69:1035s-45s. doi: 10.1093/ajcn/69.5.1035s.
24. Aagaard K, Ma J, Antony KM, Ganu R, Petrosino J, Versalovic J. The placenta harbors a unique microbiome. *Sci Transl Med.* 2014;6:237ra265. doi: 10.1126/scitranslmed.3008599.

Supplementary Figures

	Quartile for miso soup intake			
	1 (low) (n = 19,191)	2 (n = 15,559)	3 (n = 20,405)	4 (high) (n = 18,367)
Maternal age, mean (SD)	30.9 (5.1)	30.9 (5.0)	31.4 (4.8)	31.2 (4.9)
Previous deliveries, n (%)				
Nulliparous	9,220 (49.5)	6,783 (44.8)	8,374 (42.2)	7,152 (39.8)
Multiparous	9,426 (50.6)	8,376 (55.3)	11,494 (57.9)	10,829 (60.2)
Energy intake (kcal), mean (SD)	1,604 (746.4)	1,691 (754.5)	1,746 (675.7)	1,870 (851.6)
Folic acid (mg), mean (SD)	0.2 (0.2)	0.2 (0.2)	0.3 (0.1)	0.3 (0.2)
Physical activity (MET·h/day), mean (SD)	4.1 (8.5)	3.9 (8.0)	3.7 (7.8)	4.0 (8.6)
Antibacterial drug intake, n (%)				
No	17,258 (89.9)	13,912 (89.4)	18,199 (89.2)	16,289 (88.7)
Yes	1,933 (10.1)	1,647 (10.6)	2,206 (10.8)	2,078 (11.3)
Marital status, n (%)				
Married (including common-law marriage)	18,029 (94.8)	14,754 (95.5)	19,536 (96.4)	17,584 (96.5)
Single (never married)	816 (4.3)	587 (3.8)	598 (3.0)	528 (2.9)
Divorced or widowed	179 (0.9)	115 (0.7)	124 (0.6)	120 (0.7)
Pre-pregnancy BMI (kg/m²), n (%)				
<18.5	3,027 (15.8)	2,469 (15.9)	3,446 (16.9)	2,965 (16.2)
18.5 to <25	14,029 (73.2)	11,560 (74.3)	15,164 (74.4)	13,598 (74.1)
≥25	2,119 (11.1)	1,525 (9.8)	1,784 (8.8)	1,797 (9.8)
Alcohol intake (%)				
Never	6,572 (34.6)	5,226 (33.8)	6,757 (33.3)	5,952 (32.6)
Quit before learning of pregnancy	3,126 (16.4)	2,451 (15.9)	3,307 (16.3)	3,058 (16.8)
Quit after learning of pregnancy	8,804 (46.3)	7,344 (47.5)	9,687 (47.7)	8,741 (47.9)
Currently drinking	508 (2.7)	428 (2.8)	547 (2.7)	503 (2.8)
Active smoking status (%)				
Never	11,169 (58.6)	9,343 (60.4)	12,393 (61.1)	10,989 (60.1)
Quit before learning of pregnancy	4,207 (22.1)	3,467 (22.4)	4,625 (22.8)	4,177 (22.9)
Quit after learning of pregnancy	2,851 (15.0)	2,105 (13.6)	2,669 (13.2)	2,526 (13.8)
Currently smoking 10 cigarettes or less	630 (3.3)	445 (2.9)	491 (2.4)	484 (2.7)
Currently smoking more than 10 cigarettes	191 (1.0)	109 (0.7)	103 (0.5)	98 (0.5)
Passive smoking status (%)				
No one in the household smoked	9,263 (48.5)	7,627 (49.3)	10,122 (49.8)	8,710 (47.6)
Somebody smoked but not in the presence of the baby	9,377 (49.1)	7,522 (48.6)	9,768 (48.1)	9,137 (50.0)
Somebody smoked in the presence of the baby	442 (2.3)	333 (2.2)	424 (2.1)	435 (2.4)
Annual household income (JPY), n (%)				
<4 million	7,316 (41.1)	5,829 (40.0)	7,161 (37.3)	6,566 (38.6)
4–6 million	5,745 (32.3)	4,869 (33.4)	6,524 (34.0)	5,794 (34.0)
>6 million	4,747 (26.7)	3,892 (26.7)	5,500 (28.7)	4,667 (27.4)
Highest educational level, n (%)				
Junior high school or high school	6,854 (36.0)	5,212 (33.6)	6,559 (32.3)	6,579 (35.9)
Technical junior college, technical/vocational college, or associate degree	7,952 (41.8)	6,707 (43.2)	8,797 (43.3)	7,770 (42.4)
Bachelor's degree or postgraduate degree	4,211 (22.1)	3,598 (23.2)	4,980 (24.5)	3,960 (21.6)
Highest educational level of partner, n (%)				
Junior high school or high school	8,303 (44.0)	6,459 (41.9)	8,086 (39.9)	8,154 (44.7)
Technical junior college, technical/vocational college, or associate degree	4,290 (22.7)	3,540 (23.0)	4,702 (23.2)	4,033 (22.1)
Bachelor's degree or postgraduate degree	6,286 (33.3)	5,412 (35.1)	7,462 (36.9)	6,045 (33.2)
Employed, n (%)				
No	8,322 (43.9)	7,206 (46.6)	9,498 (46.9)	8,226 (45.1)
Yes	10,654 (56.1)	8,252 (53.4)	10,762 (53.1)	10,026 (54.9)

Supplementary Figure 1. Demographic and obstetric characteristics of the participants according to miso soup intake (n=73,522)

	Quartile for fermented soy bean intake			
	1 (low) (n = 13,503)	2 (n = 17,577)	3 (n = 23,265)	4 (high) (n = 19,177)
Maternal age, mean (SD)	30.6 (5.3)	30.7 (5.1)	31.3 (4.8)	31.6 (4.7)
Previous deliveries, n (%)				
Nulliparous	6,274 (47.8)	7,926 (46.3)	9,467 (41.7)	7,862 (42.0)
Multiparous	6,843 (52.2)	9,189 (53.7)	13,235 (58.3)	10,858 (58.0)
Energy intake (kcal), mean (SD)	1,540 (713.3)	1,581 (613.8)	1,726 (599.2)	1,999 (989.5)
Folic acid (mg), mean (SD)	0.2 (0.1)	0.2 (0.1)	0.3 (0.1)	0.3 (0.2)
Physical activity (MET·h/day), mean (SD)	4.0 (8.2)	3.9 (8.5)	3.7 (7.9)	4.0 (8.3)
Antibacterial drug intake, n (%)				
No	12,209 (90.4)	15,709 (89.4)	20,682 (88.9)	17,058 (89.0)
Yes	1,294 (9.6)	1,868 (10.6)	2,583 (11.1)	2,119 (11.1)
Marital status, n (%)				
Married (including common-law marriage)	12,646 (94.5)	16,575 (95.1)	22,249 (96.2)	18,433 (96.8)
Single (never married)	601 (4.5)	736 (4.2)	712 (3.1)	480 (2.5)
Divorced or widowed	132 (1.0)	127 (0.7)	158 (0.7)	121 (0.6)
Pre-pregnancy BMI (kg/m²), n (%)				
<18.5	2,253 (16.7)	2,904 (16.5)	3,785 (16.3)	2,965 (15.5)
18.5 to <25	9,707 (71.9)	12,942 (73.7)	17,352 (74.6)	14,350 (74.9)
≥25	1,535 (11.4)	1,721 (9.8)	2,115 (9.1)	1,854 (9.7)
Alcohol intake (%)				
Never	4,952 (37.2)	5,991 (34.3)	7,485 (32.4)	6,079 (31.9)
Quit before learning of pregnancy	2,248 (16.9)	2,720 (15.6)	3,672 (15.9)	3,302 (17.3)
Quit after learning of pregnancy	5,811 (43.6)	8,286 (47.4)	11,310 (48.9)	9,169 (48.1)
Currently drinking	309 (2.3)	484 (2.8)	660 (2.9)	533 (2.8)
Active smoking status (%)				
Never	8,086 (60.4)	10,257 (58.7)	14,029 (60.7)	11,522 (60.4)
Quit before learning of pregnancy	2,651 (19.8)	3,840 (22.0)	5,367 (23.2)	4,618 (24.2)
Quit after learning of pregnancy	2,019 (15.1)	2,678 (15.3)	3,023 (13.1)	2,431 (12.8)
Currently smoking 10 cigarettes or less	492 (3.7)	582 (3.3)	585 (2.5)	391 (2.1)
Currently smoking more than 10 cigarettes	151 (1.1)	119 (0.7)	125 (0.5)	106 (0.6)
Passive smoking status (%)				
No one in the household smoked	6,300 (46.9)	8,162 (46.7)	11,412 (49.3)	9,848 (51.6)
Somebody smoked but not in the presence of the baby	6,748 (50.3)	8,896 (50.9)	11,275 (48.7)	8,885 (46.6)
Somebody smoked in the presence of the baby	376 (2.8)	434 (2.5)	474 (2.1)	350 (1.8)
Annual household income (JPY), n (%)				
<4 million	5,252 (42.4)	6,639 (40.5)	8,203 (37.6)	6,778 (37.6)
4–6 million	3,983 (32.2)	5,410 (33.0)	7,439 (34.1)	6,100 (33.9)
>6 million	3,149 (25.4)	4,354 (26.5)	6,159 (28.3)	5,144 (28.5)
Highest educational level, n (%)				
Junior high school or high school	4,973 (37.3)	6,365 (36.3)	7,678 (33.1)	6,188 (32.4)
Technical junior college, technical/vocational college, or associate degree	5,470 (41.0)	7,388 (42.1)	9,997 (43.1)	8,371 (43.8)
Bachelor's degree or postgraduate degree	2,901 (21.7)	3,782 (21.6)	5,512 (23.8)	4,554 (23.8)
Highest educational level of partner, n (%)				
Junior high school or high school	6,048 (45.7)	7,720 (44.3)	9,604 (41.6)	7,630 (40.1)
Technical junior college, technical/vocational college, or associate degree	2,933 (22.2)	4,045 (23.2)	5,207 (22.6)	4,380 (23.0)
Bachelor's degree or postgraduate degree	4,258 (32.2)	5,660 (32.5)	8,280 (35.9)	7,007 (36.9)
Employed, n (%)				
No	5,986 (45.0)	7,593 (43.5)	10,630 (46.0)	9,043 (47.5)
Yes	7,326 (55.0)	9,877 (56.5)	12,483 (54.0)	10,008 (52.5)

Supplementary Figure 2. Demographic and obstetric characteristics of the participants according to soy bean intake (n=73,522)

	Quartile for yogurt intake			
	1 (low) (n = 20,129)	2 (n = 15,601)	3 (n = 16,878)	4 (high) (n = 20,914)
Maternal age, mean (SD)	30.3 (5.2)	31.0 (4.9)	31.4 (4.8)	31.8 (4.7)
Previous deliveries, n (%)				
Nulliparous	7,875 (40.0)	5,833 (38.3)	7,382 (44.8)	10,439 (51.5)
Multiparous	11,793 (60.0)	9,418 (61.8)	9,082 (55.2)	9,832 (48.5)
Energy intake (kcal), mean (SD)	1,512 (641.7)	1,677 (662.8)	1,748 (672.3)	1,960 (927.6)
Folic acid (mg), mean (SD)	0.2 (0.1)	0.2 (0.1)	0.3 (0.1)	0.3 (0.2)
Physical activity (MET·h/day), mean (SD)	4.1 (8.9)	3.8 (7.9)	3.9 (7.9)	3.8 (8.0)
Antibacterial drug intake, n (%)				
No	17,941 (89.1)	13,871 (88.9)	15,081 (89.4)	18,765 (89.7)
Yes	2,188 (10.9)	1,730 (11.1)	1,797 (10.7)	2,149 (10.3)
Marital status, n (%)				
Married (including common-law marriage)	18,820 (94.3)	14,812 (95.7)	16,127 (96.2)	20,144 (97.0)
Single (never married)	916 (4.6)	544 (3.5)	537 (3.2)	532 (2.6)
Divorced or widowed	226 (1.1)	122 (0.8)	97 (0.6)	93 (0.5)
Pre-pregnancy BMI (kg/m²), n (%)				
<18.5	3,273 (16.3)	2,490 (16.0)	2,705 (16.0)	3,439 (16.5)
18.5 to <25	14,434 (71.8)	11,510 (73.8)	12,617 (74.8)	15,790 (75.5)
≥25	2,411 (12.0)	1,593 (10.2)	1,548 (9.2)	1,673 (8.0)
Alcohol intake (%)				
Never	6,798 (34.1)	5,355 (34.5)	5,568 (33.2)	6,786 (32.7)
Quit before learning of pregnancy	3,304 (16.6)	2,556 (16.5)	2,665 (15.9)	3,417 (16.4)
Quit after learning of pregnancy	9,178 (46.0)	7,148 (46.1)	8,105 (48.3)	10,145 (48.8)
Currently drinking	655 (3.3)	457 (3.0)	437 (2.6)	437 (2.1)
Active smoking status (%)				
Never	10,395 (52.1)	9,213 (59.4)	10,492 (62.5)	13,794 (66.3)
Quit before learning of pregnancy	4,637 (23.2)	3,502 (22.6)	3,762 (22.4)	4,575 (22.0)
Quit after learning of pregnancy	3,744 (18.8)	2,213 (14.3)	2,111 (12.6)	2,083 (10.0)
Currently smoking 10 cigarettes or less	926 (4.6)	481 (3.1)	350 (2.1)	293 (1.4)
Currently smoking more than 10 cigarettes	263 (1.3)	105 (0.7)	64 (0.4)	69 (0.3)
Passive smoking status (%)				
No one in the household smoked	8,428 (42.1)	7,164 (46.1)	8,603 (51.2)	11,527 (55.4)
Somebody smoked but not in the presence of the baby	10,905 (54.5)	7,999 (51.5)	7,874 (46.9)	9,026 (43.3)
Somebody smoked in the presence of the baby	678 (3.4)	365 (2.4)	320 (1.9)	271 (1.3)
Annual household income (JPY), n (%)				
<4 million	8,749 (47.4)	5,899 (40.6)	5,838 (36.8)	6,386 (32.4)
4–6 million	5,812 (31.5)	4,883 (33.6)	5,366 (33.8)	6,871 (34.8)
>6 million	3,909 (21.2)	3,761 (25.9)	4,655 (29.4)	6,481 (32.8)
Highest educational level, n (%)				
Junior high school or high school	8,922 (44.8)	5,603 (36.0)	5,169 (30.7)	5,510 (26.4)
Technical junior college, technical/vocational college, or associate degree	7,657 (38.4)	6,670 (42.9)	7,457 (44.3)	9,442 (45.3)
Bachelor's degree or postgraduate degree	3,359 (16.9)	3,272 (21.1)	4,209 (25.0)	5,909 (28.3)
Highest educational level of partner, n (%)				
Junior high school or high school	10,085 (51.0)	6,960 (45.0)	6,589 (39.3)	7,368 (35.5)
Technical junior college, technical/vocational college, or associate degree	4,341 (21.9)	3,518 (22.7)	3,887 (23.2)	4,819 (23.2)
Bachelor's degree or postgraduate degree	5,356 (27.1)	4,990 (32.3)	6,293 (37.5)	8,566 (41.3)
Employed, n (%)				
No	9,408 (47.3)	7,129 (46.0)	7,506 (44.8)	9,209 (44.4)
Yes	10,502 (52.8)	8,381 (54.0)	9,264 (55.2)	11,547 (55.6)

Supplementary Figure 3. Demographic and obstetric characteristics of the participants according to yoghurt intake (n=73,522)

	Quartile for cheese intake			
	1 (low) (n = 18,657)	2 (n = 16,846)	3 (n = 20,637)	4 (high) (n = 17,382)
Maternal age, mean (SD)	30.3 (5.2)	30.8 (5.0)	31.4 (4.8)	31.9 (4.8)
Previous deliveries, n (%)				
Nulliparous	8,710 (48.0)	7,644 (46.6)	8,399 (41.7)	6,776 (40.0)
Multiparous	9,420 (52.0)	8,777 (53.5)	11,753 (58.3)	10,175 (60.0)
Energy intake (kcal), mean (SD)	1,511 (801.1)	1,607 (563.3)	1,754 (598.8)	2,049 (935.8)
Folic acid (mg), mean (SD)	0.2 (0.2)	0.2 (0.1)	0.3 (0.1)	0.3 (0.2)
Physical activity (MET·h/day), mean (SD)	4.3 (8.8)	3.8 (7.8)	3.7 (7.7)	3.8 (8.5)
Antibacterial drug intake, n (%)				
No	16,682 (89.4)	15,030 (89.2)	18,453 (89.4)	15,493 (89.1)
Yes	1,975 (10.6)	1,816 (10.8)	2,184 (10.6)	1,889 (10.9)
Marital status, n (%)				
Married (including common-law marriage)	17,369 (94.0)	15,989 (95.6)	19,801 (96.6)	16,744 (97.0)
Single (never married)	938 (5.1)	602 (3.6)	570 (2.8)	419 (2.4)
Divorced or widowed	176 (1.0)	131 (0.8)	132 (0.6)	99 (0.6)
Pre-pregnancy BMI (kg/m²), n (%)				
<18.5	3,061 (16.4)	2,689 (16.0)	3,333 (16.2)	2,824 (16.3)
18.5 to <25	13,414 (71.9)	12,402 (73.7)	15,483 (75.1)	13,052 (75.1)
≥25	2,173 (11.7)	1,747 (10.4)	1,809 (8.8)	1,496 (8.6)
Alcohol intake (%)				
Never	6,665 (36.1)	5,588 (33.4)	6,696 (32.7)	5,558 (32.2)
Quit before learning of pregnancy	3,080 (16.7)	2,661 (15.9)	3,305 (16.1)	2,896 (16.8)
Quit after learning of pregnancy	8,309 (45.0)	8,029 (48.0)	9,934 (48.4)	8,304 (48.1)
Currently drinking	423 (2.3)	468 (2.8)	571 (2.8)	524 (3.0)
Active smoking status (%)				
Never	10,285 (55.6)	9,913 (59.2)	12,844 (62.6)	10,852 (62.8)
Quit before learning of pregnancy	3,998 (21.6)	3,772 (22.5)	4,580 (22.3)	4,126 (23.9)
Quit after learning of pregnancy	3,296 (17.8)	2,446 (14.6)	2,543 (12.4)	1,866 (10.8)
Currently smoking 10 cigarettes or less	740 (4.0)	503 (3.0)	445 (2.2)	362 (2.1)
Currently smoking more than 10 cigarettes	196 (1.1)	110 (0.7)	119 (0.6)	76 (0.4)
Passive smoking status (%)				
No one in the household smoked	8,124 (43.8)	7,901 (47.1)	10,363 (50.4)	9,334 (54.0)
Somebody smoked but not in the presence of the baby	9,869 (53.2)	8,457 (50.4)	9,802 (47.7)	7,676 (44.4)
Somebody smoked in the presence of the baby	551 (3.0)	412 (2.5)	384 (1.9)	287 (1.7)
Annual household income (JPY), n (%)				
<4 million	7,769 (45.7)	6,252 (39.8)	7,205 (37.0)	5,646 (34.4)
4–6 million	5,239 (30.8)	5,256 (33.4)	6,677 (34.3)	5,760 (35.1)
>6 million	3,998 (23.5)	4,208 (26.8)	5,590 (28.7)	5,010 (30.5)
Highest educational level, n (%)				
Junior high school or high school	8,019 (43.4)	6,087 (36.2)	6,343 (30.8)	4,755 (27.4)
Technical junior college, technical/vocational college, or associate degree	7,371 (39.9)	7,060 (42.0)	9,072 (44.1)	7,723 (44.6)
Bachelor's degree or postgraduate degree	3,096 (16.8)	3,648 (21.7)	5,153 (25.1)	4,852 (28.0)
Highest educational level of partner, n (%)				
Junior high school or high school	9,067 (49.5)	7,381 (44.2)	8,091 (39.5)	6,463 (37.4)
Technical junior college, technical/vocational college, or associate degree	4,031 (22.0)	3,852 (23.1)	4,769 (23.3)	3,913 (22.7)
Bachelor's degree or postgraduate degree	5,234 (28.6)	5,464 (32.7)	7,618 (37.2)	6,889 (39.9)
Employed, n (%)				
No	8,096 (43.9)	7,459 (44.6)	9,527 (46.5)	8,170 (47.3)
Yes	10,336 (56.1)	9,283 (55.5)	10,974 (53.5)	9,101 (52.7)

Supplementary Figure 4. Demographic and obstetric characteristics of the participants according to cheese intake (n=73,522)

	No. of participants	No. of delayed cases (%)	Communication			Adjusted OR	(95% CI)	p-value	
			Crude OR	(95% CI)	p-value				
Miso soup									
Q1 (0–25)	19,191	750	(3.91)	reference		reference			
Q2 (25–74)	15,559	468	(3.01)	0.77	(0.68 , 0.87)	<.0001	0.75	(0.66 , 0.85)	<.0001
Q3 (74–130)	20,405	743	(3.64)	0.94	(0.85 , 1.04)	0.251	0.96	(0.85 , 1.07)	0.441
Q4 (130–2063)	18,367	518	(2.82)	0.73	(0.65 , 0.82)	<.0001	0.78	(0.69 , 0.89)	0.0001
Trend test						<.0001			0.010
Fermented soy beans									
Q1 (0–2)	13,503	522	(3.87)	reference		reference			
Q2 (2–7)	17,577	611	(3.48)	0.90	(0.80 , 1.02)	0.086	0.97	(0.85 , 1.11)	0.643
Q3 (7–13)	23,265	727	(3.12)	0.81	(0.72 , 0.91)	0.001	0.88	(0.77 , 1.00)	0.044
Q4 (13–600)	19,177	619	(3.23)	0.84	(0.75 , 0.95)	0.006	1.00	(0.87 , 1.15)	0.980
Trend test						0.002			0.556
Yogurt									
Q1 (0–10)	20,129	658	(3.27)	reference		reference			
Q2 (10–28)	15,601	500	(3.20)	1.01	(0.89 , 1.14)	0.936	0.93	(0.81 , 1.06)	0.278
Q3 (28–92)	16,878	577	(3.42)	1.08	(0.96 , 1.21)	0.209	0.98	(0.86 , 1.12)	0.785
Q4 (92–1440)	20,914	744	(3.56)	1.12	(1.00 , 1.26)	0.044	0.93	(0.82 , 1.06)	0.295
Trend test						0.018			0.464
Cheese									
Q1 (0–1)	18,657	627	(3.36)	reference		reference			
Q2 (1–2)	16,846	553	(3.28)	0.99	(0.88 , 1.12)	0.919	0.94	(0.83 , 1.08)	0.385
Q3 (2–5)	20,637	706	(3.42)	1.04	(0.93 , 1.17)	0.469	1.01	(0.89 , 1.15)	0.849
Q4 (5–240)	17,382	593	(3.41)	1.02	(0.91 , 1.15)	0.710	1.00	(0.88 , 1.15)	0.984
Trend test						0.585			0.840

Supplementary Figure 5. Odds ratios (95% confidence intervals) for relationships between the development of communication skills at the age of 1 year and the intake of fermented food during pregnancy.

†Adjusted for intake of energy, intake of folic acid, maternal age, marital status, annual household income, highest educational level, employment status for women during mid-late pregnancy, alcohol intake in mid-late pregnancy, active smoking status 1 month after delivery, passive smoking status at 1 month after delivery, physical activity during mid-late pregnancy (MET/min), pre-pregnancy BMI, previous deliveries (none, or one or more), period of gestation, sex of child, any congenital anomaly of the child, birth weight, highest educational level of partner, delivery method (vaginal delivery or caesarean section), intake of antibacterial drugs.

Bold indicates significance ($p < 0.05$)

	No. of participants	No. of delayed cases (%)	Gross motor			Adjusted OR	(95% CI)	p-value	
			Crude OR	(95% CI)	p-value				
Miso soup									
Q1 (0–25)	19,191	1,102	(5.74)	reference		reference			
Q2 (25–74)	15,559	867	(5.57)	0.97	(0.88 , 1.06)	0.450	0.94	(0.84 , 1.04)	0.195
Q3 (74–130)	20,405	1,217	(5.96)	1.03	(0.95 , 1.13)	0.442	1.03	(0.94 , 1.13)	0.527
Q4 (130–2063)	18,367	1,094	(5.96)	1.04	(0.95 , 1.13)	0.397	1.03	(0.94 , 1.14)	0.535
Trend test						0.234			0.267
Fermented soy beans									
Q1 (0–2)	13,503	759	(5.62)	reference		reference			
Q2 (2–7)	17,577	1,042	(5.93)	1.06	(0.96 , 1.16)	0.273	1.07	(0.96 , 1.19)	0.236
Q3 (7–13)	23,265	1,374	(5.91)	1.04	(0.95 , 1.14)	0.424	1.07	(0.97 , 1.19)	0.181
Q4 (13–600)	19,177	1,105	(5.76)	0.99	(0.90 , 1.09)	0.838	0.99	(0.89 , 1.11)	0.886
Trend test						0.595			0.756
Yogurt									
Q1 (0–10)	20,129	1,109	(5.51)	reference		reference			
Q2 (10–28)	15,601	844	(5.41)	0.98	(0.89 , 1.08)	0.704	0.93	(0.84 , 1.04)	0.190
Q3 (28–92)	16,878	988	(5.85)	1.07	(0.98 , 1.17)	0.154	0.99	(0.90 , 1.10)	0.878
Q4 (92–1440)	20,914	1,339	(6.40)	1.18	(1.08 , 1.28)	0.0002	1.06	(0.96 , 1.16)	0.286
Trend test						<.0001			0.166
Cheese									
Q1 (0–1)	18,657	1,072	(5.75)	reference		reference			
Q2 (1–2)	16,846	981	(5.82)	1.01	(0.92 , 1.10)	0.900	0.99	(0.90 , 1.10)	0.892
Q3 (2–5)	20,637	1,186	(5.75)	0.98	(0.90 , 1.07)	0.705	0.94	(0.85 , 1.04)	0.220
Q4 (5–240)	17,382	1,041	(5.99)	1.00	(0.91 , 1.10)	0.976	0.93	(0.84 , 1.04)	0.187
Trend test						0.761			0.087

Supplementary Figure 6. Odds ratios (95% confidence intervals) for relationships between the development of gross motor skills at the age of 1 year and the intake of fermented food during pregnancy.

†Adjusted for intake of energy, intake of folic acid, maternal age, marital status, annual household income, highest educational level, employment status for women during mid-late pregnancy, alcohol intake in mid-late pregnancy, active smoking status 1 month after delivery, passive smoking status at 1 month after delivery, physical activity during mid-late pregnancy (MET/min), pre-pregnancy BMI, previous deliveries (none, or one or more), period of gestation, sex of child, any congenital anomaly of the child, birth weight, highest educational level of partner, delivery method (vaginal delivery or caesarean section), intake of antibacterial drugs.

Bold indicates significance ($p < 0.05$)

	Fine motor							
	No. of participants	No. of delayed cases (%)	Crude OR	(95% CI)	<i>p</i> -value	Adjusted OR	(95% CI)	<i>p</i> -value
Miso soup								
Q1 (0–25)	19,191	1,187 (6.19)	reference			reference		
Q2 (25–74)	15,559	881 (5.66)	0.93	(0.85 , 1.02)	0.108	0.96	(0.87 , 1.06)	0.392
Q3 (74–130)	20,405	1,201 (5.89)	0.98	(0.90 , 1.07)	0.638	1.00	(0.91 , 1.09)	0.947
Q4 (130–2063)	18,367	1,085 (5.91)	0.99	(0.91 , 1.08)	0.783	1.01	(0.92 , 1.12)	0.796
Trend test					0.998			0.694
Fermented soy beans								
Q1 (0–2)	13,503	890 (6.59)	reference			reference		
Q2 (2–7)	17,577	1,098 (6.25)	0.96	(0.87 , 1.05)	0.355	0.98	(0.88 , 1.08)	0.681
Q3 (7–13)	23,265	1,295 (5.57)	0.86	(0.79 , 0.94)	0.001	0.87	(0.79 , 0.96)	0.007
Q4 (13–600)	19,177	1,071 (5.58)	0.87	(0.79 , 0.96)	0.005	0.90	(0.80 , 1.00)	0.046
Trend test					0.001			0.008
Yogurt								
Q1 (0–10)	20,129	1,271 (6.31)	reference			reference		
Q2 (10–28)	15,601	923 (5.92)	0.99	(0.90 , 1.08)	0.775	0.97	(0.88 , 1.07)	0.559
Q3 (28–92)	16,878	979 (5.80)	0.98	(0.90 , 1.07)	0.633	0.99	(0.90 , 1.10)	0.886
Q4 (92–1440)	20,914	1,181 (5.65)	0.95	(0.87 , 1.04)	0.267	0.96	(0.87 , 1.06)	0.379
Trend test					0.278			0.463
Cheese								
Q1 (0–1)	18,657	1,223 (6.56)	reference			reference		
Q2 (1–2)	16,846	1,035 (6.14)	0.95	(0.87 , 1.03)	0.232	0.94	(0.85 , 1.03)	0.203
Q3 (2–5)	20,637	1,148 (5.56)	0.87	(0.80 , 0.95)	0.001	0.83	(0.76 , 0.92)	0.0002
Q4 (5–240)	17,382	948 (5.45)	0.86	(0.78 , 0.94)	0.001	0.83	(0.74 , 0.92)	0.0003
Trend test					0.0001			<.0001

Supplementary Figure 7. Odds ratios (95% confidence intervals) for relationships between the development of fine motor skills at the age of 1 year and the intake of fermented food during pregnancy.

†Adjusted for intake of energy, intake of folic acid, maternal age, marital status, annual household income, highest educational level, employment status for women during mid-late pregnancy, alcohol intake in mid-late pregnancy, active smoking status 1 month after delivery, passive smoking status at 1 month after delivery, physical activity during mid-late pregnancy (MET/min), pre-pregnancy BMI, previous deliveries (none, or one or more), period of gestation, sex of child, any congenital anomaly of the child, birth weight, highest educational level of partner, delivery method (vaginal delivery or caesarean section), intake of antibacterial drugs.

Bold indicates significance ($p < 0.05$)

	No. of participants	No. of delayed cases (%)	Problem-solving			Adjusted OR	(95% CI)	p-value
			Crude OR	(95% CI)	p-value			
Miso soup								
Q1 (0–25)	19,191	1,090 (5.68)		reference		reference		
Q2 (25–74)	15,559	854 (5.49)	0.99	(0.90 , 1.08)	0.742	1.00	(0.90 , 1.11)	0.968
Q3 (74–130)	20,405	1,047 (5.13)	0.93	(0.85 , 1.01)	0.091	0.95	(0.86 , 1.05)	0.340
Q4 (130–2063)	18,367	980 (5.34)	0.97	(0.89 , 1.06)	0.499	1.04	(0.94 , 1.15)	0.475
Trend test					0.276			0.787
Fermented soy beans								
Q1 (0–2)	13,503	848 (6.28)		reference		reference		
Q2 (2–7)	17,577	955 (5.43)	0.87	(0.79 , 1.00)	0.005	0.89	(0.80 , 1.00)	0.040
Q3 (7–13)	23,265	1,183 (5.08)	0.83	(0.76 , 0.91)	<.0001	0.87	(0.78 , 0.96)	0.007
Q4 (13–600)	19,177	985 (5.14)	0.84	(0.76 , 0.93)	0.001	0.94	(0.84 , 1.05)	0.244
Trend test					0.0004			0.176
Yogurt								
Q1 (0–10)	20,129	1,132 (5.62)		reference		reference		
Q2 (10–28)	15,601	813 (5.21)	0.99	(0.90 , 1.09)	0.787	0.94	(0.85 , 1.05)	0.276
Q3 (28–92)	16,878	885 (5.24)	1.01	(0.92 , 1.11)	0.890	0.91	(0.82 , 1.01)	0.082
Q4 (92–1440)	20,914	1,141 (5.46)	1.05	(0.96 , 1.15)	0.266	0.96	(0.86 , 1.06)	0.400
Trend test					0.206			0.344
Cheese								
Q1 (0–1)	18,657	1,128 (6.05)		reference		reference		
Q2 (1–2)	16,846	943 (5.60)	0.94	(0.86 , 1.03)	0.178	0.95	(0.86 , 1.05)	0.321
Q3 (2–5)	20,637	1,036 (5.02)	0.85	(0.77 , 0.93)	0.0002	0.86	(0.78 , 0.95)	0.003
Q4 (5–240)	17,382	864 (4.97)	0.83	(0.76 , 0.92)	0.0002	0.88	(0.79 , 0.99)	0.027
Trend test					<.0001			0.002

Supplementary Figure 8. Odds ratios (95% confidence intervals) for relationships between the development of problem-solving skills at the age of 1 year and the intake of fermented food during pregnancy.

†Adjusted for intake of energy, intake of folic acid, maternal age, marital status, annual household income, highest educational level, employment status for women during mid-late pregnancy, alcohol intake in mid-late pregnancy, active smoking status 1 month after delivery, passive smoking status at 1 month after delivery, physical activity during mid-late pregnancy (MET/min), pre-pregnancy BMI, previous deliveries (none, or one or more), period of gestation, sex of child, any congenital anomaly of the child, birth weight, highest educational level of partner, delivery method (vaginal delivery or caesarean section), intake of antibacterial drugs.

Bold indicates significance ($p < 0.05$)

	No. of participants	No. of delayed cases (%)	Personal-social			Adjusted OR	(95% CI)	p-value
			Crude OR	(95% CI)	p-value			
Miso soup								
Q1 (0–25)	19,191	599 (3.12)	reference			reference		
Q2 (25–74)	15,559	458 (2.94)	0.95	(0.84 , 1.08)	0.413	0.96	(0.84 , 1.10)	0.531
Q3 (74–130)	20,405	643 (3.15)	1.02	(0.91 , 1.14)	0.724	1.02	(0.90 , 1.16)	0.769
Q4 (130–2063)	18,367	529 (2.88)	0.92	(0.82 , 1.04)	0.181	0.90	(0.78 , 1.03)	0.109
Trend test					0.367			0.213
Fermented soy beans								
Q1 (0–2)	13,503	412 (3.05)	reference			reference		
Q2 (2–7)	17,577	544 (3.09)	1.03	(0.90 , 1.17)	0.691	1.04	(0.90 , 1.20)	0.611
Q3 (7–13)	23,265	671 (2.88)	0.97	(0.86 , 1.11)	0.681	0.96	(0.84 , 1.11)	0.572
Q4 (13–600)	19,177	602 (3.14)	1.08	(0.94 , 1.23)	0.268	1.08	(0.93 , 1.25)	0.312
Trend test					0.434			0.615
Yogurt								
Q1 (0–10)	20,129	653 (3.24)	reference			reference		
Q2 (10–28)	15,601	491 (3.15)	0.99	(0.87 , 1.11)	0.817	0.96	(0.84 , 1.09)	0.502
Q3 (28–92)	16,878	484 (2.87)	0.89	(0.79 , 1.01)	0.062	0.86	(0.75 , 0.98)	0.027
Q4 (92–1440)	20,914	601 (2.87)	0.88	(0.79 , 1.00)	0.041	0.87	(0.76 , 0.99)	0.039
Trend test					0.023			0.021
Cheese								
Q1 (0–1)	18,657	597 (3.20)	reference			reference		
Q2 (1–2)	16,846	511 (3.03)	0.95	(0.84 , 1.08)	0.430	0.94	(0.82 , 1.07)	0.334
Q3 (2–5)	20,637	600 (2.91)	0.92	(0.82 , 1.04)	0.187	0.85	(0.74 , 0.97)	0.015
Q4 (5–240)	17,382	521 (3.00)	0.97	(0.85 , 1.10)	0.589	0.89	(0.77 , 1.03)	0.114
Trend test					0.455			0.036

Supplementary Figure 9. Odds ratios (95% confidence intervals) for relationships between the development of personal-social skills at the age of 1 year and the intake of fermented food during pregnancy.

†Adjusted for intake of energy, intake of folic acid, maternal age, marital status, annual household income, highest educational level, employment status for women during mid-late pregnancy, alcohol intake in mid-late pregnancy, active smoking status 1 month after delivery, passive smoking status at 1 month after delivery, physical activity during mid-late pregnancy (MET/min), pre-pregnancy BMI, previous deliveries (none, or one or more), period of gestation, sex of child, any congenital anomaly of the child, birth weight, highest educational level of partner, delivery method (vaginal delivery or caesarean section), intake of antibacterial drugs.

Bold indicates significance ($p < 0.05$)