学位論文

Association between consumption of fermented foods and sleep duration of children：the Japan Environment and Children's Study

発酵食品の摂取と児の睡眠時間との関連：

子どもの健康と環境に関する全国調査

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Contents

Introduction

Association between consumption of fermented foods and sleep duration of children: the Japan Environment and Children's Study

It has been reported that balanced nutrition and adequate and good sleep time are essential for children's healthy growth, and that they interact with each other [1]. In particular, from the neonatal period to infancy, children sleep longer than adults because of their development and age-appropriate sleep duration [2]. Sleep deprivation has been reported to adversely affect neurocognitive and neurobehavior, mood and emotional issues and specific conditions, like pulmonary hypertension, physical and neurological development [3-9]. In addition to diet and living environment, lack of sleep has been suggested as one of the causes of obesity, which is currently increasing worldwide [10].

Previous studies have shown that probiotic-containing foods and fermented foods are gaining attention due to their positive effects on the gut microbiota [11, 12], and a good gut microbiota has a positive effect on sleep [13, 14]. Furthermore, it has been suggested that the mother's diet and intestinal bacteria during pregnancy are transmitted to the unborn child and affect the child's health after birth [15]. Epidemiological studies conducted to date have also reported that children born to mothers who consumed a large amount of miso soup during pregnancy are associated with a reduced risk of sleep deprivation at the age of 1 year [16]. As described above, it is predicted that active intake of fermented foods improves the intestinal microflora, and that a good intestinal microflora is associated with a reduced risk of sleep deprivation, which is influenced from the time the child is in the mother's body. However, the long-term association between fermented foods consumed by the mother during pregnancy and reduced risk of sleep deprivation in the child has not been examined. It is also expected that as the child grows up, the child's own intake of foods will have a stronger influence on the child's sleep than the foods inoculated by the mother during pregnancy. But no large-scale study has been conducted on the relationship between the child's own intake of fermented foods and sleep after birth.

The doctoral dissertation is based on two papers [17, 18].

First division

Association between maternal fermented food consumption and child sleep duration at the age of 3 years: the Japan Environment and Children's Study

Abstract

Background: Using cohort data from the Japan Environment and Children's Study (JECS), Sugimori et al reported that the risk of sleep deprivation in 1-year-old children was reduced with a higher intake of fermented foods, particularly miso. The present study, which evaluates children from the same cohort at 3 years of age, is a continuation of that work.

Methods: After excluding from the JECS dataset comprising 104,062 records, I evaluated 64,200 mother-child pairs, wherein the child was 3 years old. I examined the association of dietary intake of fermented foods during pregnancy with child sleep duration of < 10 h at the age of 3 years.

Results: Multivariable logistic regression analysis with the lowest quartiles used as a reference revealed adjusted odds ratios with 95% confidence intervals (CIs) for the second through fourth quintiles of 0.98 (95% CI: 0.90-1.06), 0.93 (0.85-1.01), and 0.85 (0.78-0.94), and 0.82 (0.76-0.88) for cheese intake.

Conclusions: The consumption of fermented foods during pregnancy is also associated with sleep deprivation in 3-year-old children, albeit in a limited way.

Keywords: Probiotics, Child, Sleep, Circadian rhythm, Cheese, Health

Background

Children need a sufficient amount of good-quality sleep for healthy development. From the neonatal period to infancy and then early childhood, sleep patterns change with the child's development. Short sleep duration has been reported to negatively affect physical and neurological development, including obesity in infancy and childhood [19, 20] and hyperactivity at 6 years of age [21]. Therefore, it is important to investigate the risk factors for sleep deprivation in children.

One of the factors that affect children is the diet of their mothers during pregnancy, which is recognized as a lifestyle factor. For example, probiotic-containing and fermented foods are thought to influence the gut microbiota [11] and have received considerable interest because they are associated with maternal health [22, 23] or, conversely, the development of diseases [24, 15], depending on the amount consumed. It has also been reported that children born by cesarean section are at higher risk of mental and developmental disorders, and one possible reason for this is that they are not exposed to their mother's gut bacteria at birth. With respect to the reported association between the microbiota at 1 year of age and neurocognitive development at 1 and 2 years of age [25, 26], maternal intake of fermented foods has been suggested to influence the normal development of children, especially sleep duration. In particular, the intestinal microbiota of children changes significantly from the neonatal period through infancy and weaning and stabilizes at around 3 years of year, reaching a composition similar to that of adults[27, 28]. In other words, vertical transmission of intestinal bacteria of maternal origin and maternal diet are predicted to affect the intestinal microbiota of children, but the association between maternal intake of fermented foods and children's sleep duration has not been examined on a large scale in epidemiological studies.

Against this background, Sugimori et al examined the association of maternal food intake preferences during pregnancy with infant sleep duration [16]. Specifically, using data from approximately 70,000 mother–infant pairs from a large cohort study, the Japan Environment and Children's Study (JECS), They investigated the association between fermented food intake during pregnancy and infant sleep during the first postpartum year. They found that the higher the intake of fermented foods, especially miso soup, the more likely it is for the infant to sleep for at least 11 h. However, because the child's brain grows exponentially until 2 years of age [29], it is important to clarify whether this association with fermented food persists beyond that point.

Therefore, to expand on these recent findings [16], I investigated whether maternal fermented food intake during pregnancy was associated with the sleep deprivation of children in the same cohort at 3 years of age.

Methods

Study population

The JECS protocol has been described elsewhere [30, 31]. In short, the JECS is a nationwide government-funded birth cohort study that aims to determine the associations of various environmental factors with child health and development. JECS participants are women residing in 15 regions of Japan who were enrolled during the first trimester of pregnancy between January 2011 and March 2014 [30, 31]. Follow-ups were conducted during the second or third trimester, at childbirth, and at 1 month postpartum during scheduled in-hospital checkups. Subsequent follow-ups were conducted at 12 and 36 months postpartum by mail.

The present study analyzed the jecs-ta-20190930 dataset released in October 2019, which comprises 104,062 records obtained from a questionnaire-based survey of the participants. I excluded 3,758 cases that resulted in miscarriage or stillbirth and 1,891 cases of multiple births to focus on typical pregnancies (Figure 1). Additionally, I also excluded 33,790 records because of incomplete responses to the questionnaire and 423 records for children whose sleep duration was recorded as 0, leaving 64,200 questionnaires with all data available for the final analysis.

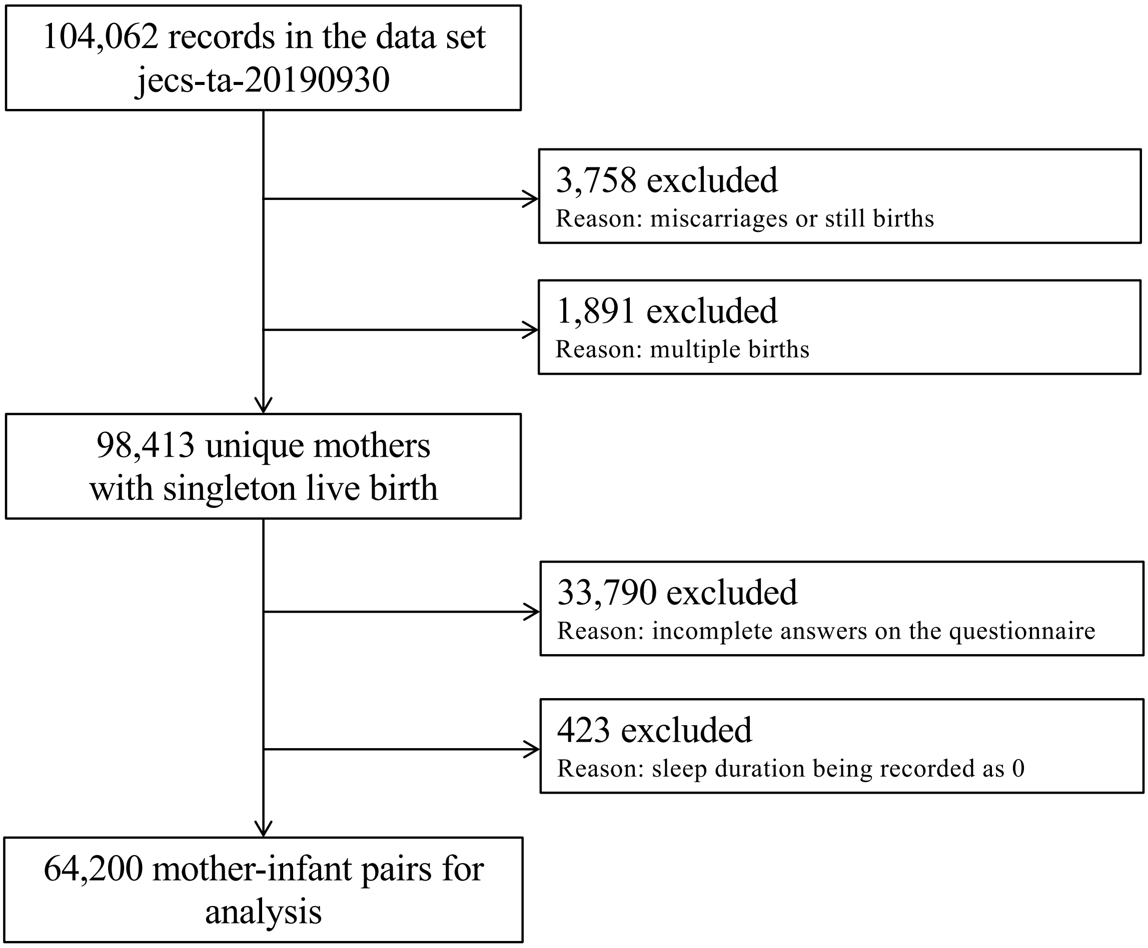

Figure 1. Flow diagram of the recruitment and exclusion process for participants

Data assessment

Exposure

Dietary intake of fermented foods during pregnancy (from the discovery of pregnancy to the second or third trimester) was assessed using a food frequency questionnaire (FFQ) [32]. Fermented foods were foods such as cheese and yogurt, the preparation of which involves fermentation of food ingredients by microorganisms. This FFQ is a semi-quantitative instrument that assesses the average consumption of 171 food and beverage items. The FFQ includes four fermented foods: miso soup (made with miso, a Japanese traditional fermented seasoning), yogurt, cheese, and natto (Japanese fermented soybeans). The FFQ has not been validated specifically for pregnant women but has been validated in a large epidemiological study of adults in the general population and has already been used in a number of the JECS studies[33-35]. In this FFQ, participants were asked how often they consumed each food type and how much of it they consumed from learning of the pregnancy to the present. For miso soup, six frequency categories were used to record overall consumption frequency (from almost never to every day), nine frequency categories were used to record the daily consumption frequency (from < 1 time to ≥ 10 times), and five categories were used to report the taste of the miso soup (from very bland to very strong), which was taken to indicate the amount of miso in the soup. The daily intake (g/day) of miso was then calculated by multiplying the overall consumption frequency by the daily consumption frequency by a factor based on the reported taste. For the other three fermented foods—yogurt, cheese, and natto—the standard portion size for each food type was categorized as small (50% smaller than standard), medium (same as standard), or large (50% larger than standard). Nine frequency categories for each item were used to record consumption frequency (< 1 time/month to ≥ 7 times/day).

The daily intake of each of these three fermented foods was calculated by multiplying the consumption frequency by the standard portion size. Then, participants were categorized by quartile of intake amount (g/day) for each of the four fermented foods.

Outcome

To measure child sleep duration at 3 years after childbirth, parents were instructed to indicate when their child slept on the previous day. Parents marked the times when their child was asleep by drawing lines through boxes, indicating 30-min intervals, for the 24-h period beginning from 12:00 am at the start of the previous day.

Sleep duration of 10–13 h in a 24-h period is recommended for 3-year-old children by the United States National Sleep Foundation [2]. Therefore, I selected 10 h as the lower limit of the appropriate sleep duration and defined children sleeping less than this amount as having sleep deprivation.

Covariates

The covariates adjusted for were energy intake during pregnancy as assessed using the FFQ [32], maternal age during pregnancy, previous childbirth, body mass index (BMI) at 1 month after childbirth, maternal education level, annual household income during pregnancy, marital status at 6 months after childbirth, alcohol intake at 1 month after childbirth, smoking status at 1 month after childbirth, employment status at 1 year after childbirth, sex of the child, child attendance at nursery at 1 year after childbirth, the location where the child slept at night at 1 year after childbirth, birth weight, gestational age, consumption of dairy products at 3 years after childbirth, presence of any disease up to 3 years after childbirth, and date (month) of birth. These variables were categorized as in sugimori et al study [16].

Statistical analyses

Unless otherwise stated, data are expressed as the mean ± standard deviation or median.

Odds ratios (ORs) and 95% confidence intervals (95% CIs) for the risk of sleep deprivation according to each fermented food intake were calculated using logistic regression analysis, with each lowest quartile used as a reference. Adjusted ORs were calculated using all of the covariates described in the previous section, whereas crude ORs were calculated without adjustment for any covariates. In trend tests, categorical numbers were assigned to the quartile distributions for each fermented food intake and were treated as continuous variables. A two-sided p-value of < 0.05 was regarded as statistically significant. Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Additional Analysis

To determine the association between overall fermented food intake during pregnancy and the sleep of their children at 3 years of age, I calculated the total score for quartiles of each of miso, yogurt, cheese, and natto during pregnancy, where the first quartile counted as 1 point, the second quartile as 2 points, and so forth. Thus, the score for the overall intake of fermented foods ranged from 4 to 16 points. The total score was also further categorized into quartiles. Analysis was likewise calculated using logistic regression analysis to obtain ORs and 95% CIs, setting the lowest quartile as the reference group.

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). The JECS is conducted in accordance with the Helsinki Declaration and other national regulations, and written informed consent was obtained from the parents/guardians of participants under 16 years of age.

Results

Table 1 shows maternal characteristics according to the quartile of cheese intake during pregnancy. Participants with higher cheese intake were more likely to have high energy intake, to be older, to be multiparous, to have a normal weight (BMI: 18.5–<25), to have a higher education level, to have a higher household income, to be a nonsmoker, to be unemployed, and to send their child to a nursery. Table 2 shows maternal characteristics according to the quartile of miso intake during pregnancy. Participants with higher miso intake were more likely to be multiparous and nonsmokers, and less likely to send their child to a nursery. Tables 3 and 4 show maternal characteristics according to quartiles of yogurt and natto intake during pregnancy, which were similar to those for cheese intake.

Compared with the excluded participants (n = 30,613), the included mothers (n = 64,200) were more likely to eat yogurt, cheese, and natto; to be older; to be married; to be a nonsmoker; to have a higher education level; to have a higher income; to be within the normal range of BMI; to be primiparas; and to have female infants with a heavier birth weight and longer gestational age.

Table 1. Characteristics according to quartile for cheese intake during pregnancy in women (N = 64,200).

		Quartile of cheese intake									
		1 (low)		2		3		4 (high)		Total	
Median intake of cheese, g/day		0.0		1.3		4.3		10.0			
Mean intake of energy, cal		1,534		1,619		1,758		2,034		1,736	
Age at delivery, years		30.9		31.4		31.9		32.3		31.6	
Previous deliveries	Nullipara	7,090	(46.0)	7,187	(43.9)	6,748	(39.9)	5,993	(38.6)	27,018	(42.1)
	Multipara	8,314	(54.0)	9,170	(56.1)	10,164	(60.1)	9,534	(61.4)	37182	(57.9)
BMI (kg/m^2)	<18.5	783	(5.1)	779	(4.8)	859	(5.1)	797	(5.1)	3,218	(5.0)
	18.5-<25	11,979	(77.8)	13,068	(79.9)	13,752	(81.3)	12,635	(81.4)	51,434	(80.1)
	≥25	2,642	(17.2)	2,510	(15.4)	2,301	(13.6)	2,095	(13.5)	9,548	(14.9)
Highest educational level	Junior high school or high school	6,175	(40.1)	5,591	(34.2)	4,852	(28.7)	3,972	(25.6)	20,590	(32.1)
	Technical junior college, technical/vocational college or associate degree	6,443	(41.8)	7,085	(43.3)	7,554	(44.7)	6,936	(44.7)	28,018	(43.6)
	Bachelor's degree, postgraduate degree	2,786	(18.1)	3,681	(22.5)	4,506	(26.6)	4,619	(29.8)	15,592	(24.3)
Annual household income, JPY	<4 million	6,861	(44.5)	6,330	(38.7)	6,076	(35.9)	5,230	(33.7)	24,497	(38.2)
	4-6 million	4,844	(31.5)	5,577	(34.1)	5,878	(34.8)	5,487	(35.3)	21,786	(33.9)
	>6 million	3,699	(24.0)	4,450	(27.2)	4,958	(29.3)	4,810	(31.0)	17,917	(27.9)
Marital status	Married (including common law marriage)	15,107	(98.1)	16,142	(98.7)	16,728	(98.9)	15,375	(99.0)	63,352	(98.7)
	Divorced or widowed	130	(0.8)	112	(0.7)	90	(0.5)	73	(0.5)	405	(0.6)
	Others	167	(1.1)	103	(0.6)	94	(0.6)	79	(0.5)	443	(0.7)
Alcohol intake	Never	14,220	(92.3)	15,021	(91.8)	15,523	(91.8)	14,190	(91.4)	58,954	(91.8)
	Ex-drinker	618	(4.0)	692	(4.2)	788	(4.7)	703	(4.5)	2,801	(4.4)
	One to three times/month	382	(2.5)	438	(2.7)	426	(2.5)	442	(2.9)	1,688	(2.6)
	Once a week or more	184	(1.2)	206	(1.3)	175	(1.0)	192	(1.2)	757	(1.2)
Smoking status	Never	8,803	(57.2)	9,909	(60.6)	10,810	(63.9)	9,985	(64.3)	39,507	(61.5)
	Ex-drinker	3,472	(22.5)	3,786	(23.2)	3,871	(22.9)	3,728	(24.0)	14,857	(23.1)
	One to three times/month	2,413	(15.7)	2,130	(13.0)	1,827	(10.8)	1,464	(9.4)	7,834	(12.2)
	Once a week or more	716	(4.7)	532	(3.3)	404	(2.4)	350	(2.3)	2,002	(3.1)
Employed	No	7,752	(50.3)	8,395	(51.3)	8,953	(52.9)	8,471	(54.6)	33,571	(52.3)
	Yes	7,652	(49.7)	7,962	(48.7)	7,959	(47.1)	7,056	(45.4)	30,629	(47.7)
Child sex	Boy	7,504	(48.7)	8,124	(49.7)	8,171	(48.3)	7,667	(49.4)	31,466	(49.0)
	Girl	7,900	(51.3)	8,233	(50.3)	8,741	(51.7)	7,860	(50.6)	32,734	(51.0)
Nursery	No	5,354	(34.8)	5,887	(36.0)	6,248	(36.9)	5,927	(38.2)	23,416	(36.5)
	Yes	10,050	(65.2)	10,470	(64.0)	10,664	(63.1)	9,600	(61.8)	40,784	(63.5)
Location where the baby sleeps at night	In the parent's bed	12,933	(84.0)	13,719	(83.9)	14,294	(84.5)	13,019	(83.9)	53,965	(84.1)
	In a baby bed located in the parent's room	2,262	(14.7)	2,425	(14.8)	2,403	(14.2)	2,282	(14.7)	9,372	(14.6)
	In a baby bed located in a room other than the bedroom of his/her parents	152	(1.0)	145	(0.9)	161	(1.0)	173	(1.1)	631	(1.0)
	Other	57	(0.4)	68	(0.4)	54	(0.3)	53	(0.3)	232	(0.4)
Birth weight, g		3,018		3,028		3,034		3,035		3,029	
Gestational weeks		39.3		39.3		39.3		39.3		39.3	
Eating dairy products	Yes	14,971	(97.2)	15,953	(97.5)	16,502	(97.6)	15,164	(97.7)	62,590	(97.5)
	No	433	(2.8)	404	(2.5)	410	(2.4)	363	(2.3)	1,610	(2.5)
Disease	No	9,111	(59.2)	9,728	(59.5)	10,024	(59.3)	9,193	(59.2)	38,056	(59.3)
	Yes	6,293	(40.9)	6,629	(40.5)	6,888	(40.7)	6,334	(40.8)	26,144	(40.7)
Birth month	1	1,259	(8.2)	1,214	(7.4)	1,285	(7.6)	1,169	(7.5)	4,927	(7.7)
	2	1,063	(6.9)	1,126	(6.9)	1,187	(7.0)	1,056	(6.8)	4,432	(6.9)
	3	1,178	(7.7)	1,285	(7.9)	1,259	(7.4)	1,188	(7.7)	4,910	(7.6)
	4	1,223	(7.9)	1,254	(7.7)	1,297	(7.7)	1,179	(7.6)	4,953	(7.7)
	5	1,202	(7.8)	1,320	(8.1)	1,400	(8.3)	1,258	(8.1)	5,180	(8.1)
	6	1,202	(7.8)	1,258	(7.7)	1,368	(8.1)	1,243	(8.0)	5,071	(7.9)
	7	1,382	(9.0)	1,477	(9.0)	1,484	(8.8)	1,414	(9.1)	5,757	(9.0)
	8	1,555	(10.1)	1,660	(10.2)	1,669	(9.9)	1,618	(10.4)	6,502	(10.1)
	9	1,568	(10.2)	1,689	(10.3)	1,683	(10.0)	1,627	(10.5)	6,567	(10.2)
	10	1,433	(9.3)	1,567	(9.6)	1,631	(9.6)	1,416	(9.1)	6,047	(9.4)
	11	1,178	(7.7)	1,251	(7.7)	1,350	(8.0)	1,177	(7.6)	4,956	(7.7)
	12	1,161	(7.5)	1,256	(7.7)	1,299	(7.7)	1,182	(7.6)	4,898	(7.6)

BMI; body mass index. JPY; Japanese Yen.

Table 2. Characteristics according to quartile for miso intake during pregnancy in women (N = 64,200).

		Quartile of miso intake									
		1 (low)		2		3		4 (high)		Total	
Median intake of miso, g/day		10.0		32.1		88.4		225.0			
Mean intake of energy, cal		1,620		1,697		1,752		1,868		1,736	
Age at delivery, years		31.4		31.4		31.9		31.7		31.6	
Previous deliveries	Nullipara	7,798	(47.6)	5,902	(43.0)	7,250	(40.3)	6,068	(37.7)	27,018	(42.1)
	Multipara	8,603	(52.5)	7,818	(57.0)	10,738	(59.7)	10,023	(62.3)	37182	(57.9)
BMI (kg/m^2)	<18.5	829	(5.1)	684	(5.0)	952	(5.3)	753	(4.7)	3,218	(5.0)
	18.5-<25	12,940	(78.9)	10,989	(80.1)	14,653	(81.5)	12,852	(79.9)	51,434	(80.1)
	≥25	2,632	(16.1)	2,047	(14.9)	2,383	(13.3)	2,486	(15.5)	9,548	(14.9)
Highest educational level	Junior high school or high school	5,491	(33.5)	4,310	(31.4)	5,412	(30.1)	5,377	(33.4)	20,590	(32.1)
	Technical junior college, technical/vocational college or associate degree	7,062	(43.1)	6,041	(44.0)	7,921	(44.0)	6,994	(43.5)	28,018	(43.6)
	Bachelor's degree, postgraduate degree	3,848	(23.5)	3,369	(24.6)	4,655	(25.9)	3,720	(23.1)	15,592	(24.3)
Annual household income, JPY	<4 million	6,579	(40.1)	5,360	(39.1)	6,511	(36.2)	6,047	(37.6)	24,497	(38.2)
	4-6 million	5,374	(32.8)	4,624	(33.7)	6,233	(34.7)	5,555	(34.5)	21,786	(33.9)
	>6 million	4,448	(27.1)	3,736	(27.2)	5,244	(29.2)	4,489	(27.9)	17,917	(27.9)
Marital status	Married (including common law marriage)	16,092	(98.1)	13,536	(98.7)	17,808	(99.0)	15,916	(98.9)	63,352	(98.7)
	Divorced or widowed	136	(0.8)	89	(0.7)	93	(0.5)	87	(0.5)	405	(0.6)
	Others	173	(1.1)	95	(0.7)	87	(0.5)	88	(0.6)	443	(0.7)
Alcohol intake	Never	14,963	(91.2)	12,574	(91.7)	16,586	(92.2)	14,831	(92.2)	58,954	(91.8)
	Ex-drinker	731	(4.5)	608	(4.4)	770	(4.3)	692	(4.3)	2,801	(4.4)
	One to three times/month	476	(2.9)	380	(2.8)	449	(2.5)	383	(2.4)	1,688	(2.6)
	Once a week or more	231	(1.4)	158	(1.2)	183	(1.0)	185	(1.2)	757	(1.2)
Smoking status	Never	9,851	(60.1)	8,525	(62.1)	11,221	(62.4)	9,910	(61.6)	39,507	(61.5)
	Ex-drinker	3,755	(22.9)	3,150	(23.0)	4,195	(23.3)	3,757	(23.4)	14,857	(23.1)
	One to three times/month	2,157	(13.2)	1,611	(11.7)	2,096	(11.7)	1,970	(12.2)	7,834	(12.2)
	Once a week or more	638	(3.9)	434	(3.2)	476	(2.7)	454	(2.8)	2,002	(3.1)
Employed	No	8,507	(51.9)	7,361	(53.7)	9,562	(53.2)	8,141	(50.6)	33,571	(52.3)
	Yes	7,894	(48.1)	6,359	(46.4)	8,426	(46.8)	7,950	(49.4)	30,629	(47.7)
Child sex	Boy	8,059	(49.1)	6,668	(48.6)	8,778	(48.8)	7,961	(49.5)	31,466	(49.0)
	Girl	8,342	(50.9)	7,052	(51.4)	9,210	(51.2)	8,130	(50.5)	32,734	(51.0)
Nursery	No	5,810	(35.4)	4,961	(36.2)	6,624	(36.8)	6,021	(37.4)	23,416	(36.5)
	Yes	10,591	(64.6)	8,759	(63.8)	11,364	(63.2)	10,070	(62.6)	40,784	(63.5)
Location where the baby sleeps at night	In the parent's bed	13,666	(83.3)	11,581	(84.4)	15,103	(84.0)	13,615	(84.6)	53,965	(84.1)
	In a baby bed located in the parent's room	2,489	(15.2)	1,960	(14.3)	2,662	(14.8)	2,261	(14.1)	9,372	(14.6)
	In a baby bed located in a room other than the bedroom of his/her parents	188	(1.2)	132	(1.0)	167	(0.9)	144	(0.9)	631	(1.0)
	Other	58	(0.4)	47	(0.3)	56	(0.3)	71	(0.4)	232	(0.4)
Birth weight, g		3,027		3,025		3,027		3,036		3,029	
Gestational weeks		39.3		39.3		39.3		39.2		39.3	
Eating dairy products	16,429	15,979	(97.4)	13,366	(97.4)	17,546	(97.5)	15,699	(97.6)	62,590	(97.5)
	504	422	(2.6)	354	(2.6)	442	(2.5)	392	(2.4)	1,610	(2.5)
Disease	10,026	9,676	(59.0)	8,074	(58.9)	10,740	(59.7)	9,566	(59.5)	38,056	(59.3)
	6,907	6,725	(41.0)	5,646	(41.2)	7,248	(40.3)	6,525	(40.6)	26,144	(40.7)
Birth month	1,392	1,140	(7.0)	1,030	(7.5)	1,418	(7.9)	1,339	(8.3)	4,927	(7.7)
	1,222	970	(5.9)	974	(7.1)	1,329	(7.4)	1,159	(7.2)	4,432	(6.9)
	1,395	1,059	(6.5)	993	(7.2)	1,491	(8.3)	1,367	(8.5)	4,910	(7.7)
	1,272	1,047	(6.4)	1,045	(7.6)	1,504	(8.4)	1,357	(8.4)	4,953	(7.7)
	1,320	1,138	(6.9)	1,094	(8.0)	1,551	(8.6)	1,397	(8.7)	5,180	(8.1)
	1,141	1,168	(7.1)	1,058	(7.7)	1,473	(8.2)	1,372	(8.5)	5,071	(7.9)
	1,334	1,450	(8.8)	1,207	(8.8)	1,595	(8.9)	1,505	(9.4)	5,757	(9.0)
	1,668	1,697	(10.4)	1,380	(10.1)	1,811	(10.1)	1,614	(10.0)	6,502	(10.1)
	1,715	1,877	(11.4)	1,433	(10.4)	1,694	(9.4)	1,563	(9.7)	6,567	(10.2)
	1,663	1,915	(11.7)	1,307	(9.5)	1,538	(8.6)	1,287	(8.0)	6,047	(9.4)
	1,389	1,510	(9.2)	1,142	(8.3)	1,264	(7.0)	1,040	(6.5)	4,956	(7.7)
	1,422	1,430	(8.7)	1,057	(7.7)	1,320	(7.3)	1,091	(6.8)	4,898	(7.6)

BMI; body mass index. JPY; Japanese Yen.

Table 3. Characteristics according to quartile for yogurt intake during pregnancy in women (N = 64,200).

		Quartile of yogurt intake									
		1 (low)		2		3		4 (high)		Total	
Median intake of yogurt, g/day		8.0		25.7		60.0		120.0			
Mean intake of energy, cal		1,536		1,680		1,750		1,949		1,736	
Age at delivery, years		30.9		31.5		31.8		32.2		31.6	
Previous deliveries	Nullipara	6,372	(37.6)	5,280	(36.5)	6,171	(43.4)	9,195	(49.5)	27,018	(42.1)
	Multipara	10,561	(62.4)	9,191	(63.5)	8,039	(56.6)	9,391	(50.5)	37182	(57.9)
BMI (kg/m^2)	<18.5	764	(4.5)	685	(4.7)	729	(5.1)	1,040	(5.6)	3,218	(5.0)
	18.5-<25	13,188	(77.9)	11,551	(79.8)	11,482	(80.8)	15,213	(81.9)	51,434	(80.1)
	≥25	2,981	(17.6)	2,235	(15.4)	1,999	(14.1)	2,333	(12.6)	9,548	(14.9)
Highest educational level	Junior high school or high school	7,068	(41.7)	4,846	(33.5)	4,066	(28.6)	4,610	(24.8)	20,590	(32.1)
	Technical junior college, technical/vocational college or associate degree	6,785	(40.1)	6,303	(43.6)	6,417	(45.2)	8,513	(45.8)	28,018	(43.6)
	Bachelor's degree, postgraduate degree	3,080	(18.2)	3,322	(23.0)	3,727	(26.2)	5,463	(29.4)	15,592	(24.3)
Annual household income, JPY	<4 million	7,796	(46.0)	5,655	(39.1)	5,141	(36.2)	5,905	(31.8)	24,497	(38.2)
	4-6 million	5,468	(32.3)	4,975	(34.4)	4,804	(33.8)	6,539	(35.2)	21,786	(33.9)
	>6 million	3,669	(21.7)	3,841	(26.5)	4,265	(30.0)	6,142	(33.1)	17,917	(27.9)
Marital status	Married (including common law marriage)	16,623	(98.2)	14,279	(98.7)	14,047	(98.9)	18,403	(99.0)	63,352	(98.7)
	Divorced or widowed	155	(0.9)	87	(0.6)	78	(0.6)	85	(0.5)	405	(0.6)
	Others	155	(0.9)	105	(0.7)	85	(0.6)	98	(0.5)	443	(0.7)
Alcohol intake	Never	15,258	(90.1)	13,260	(91.6)	13,104	(92.2)	17,332	(93.3)	58,954	(91.8)
	Ex-drinker	852	(5.0)	632	(4.4)	612	(4.3)	705	(3.8)	2,801	(4.4)
	One to three times/month	530	(3.1)	413	(2.9)	352	(2.5)	393	(2.1)	1,688	(2.6)
	Once a week or more	293	(1.7)	166	(1.2)	142	(1.0)	156	(0.8)	757	(1.2)
Smoking status	Never	9,130	(53.9)	8,798	(60.8)	9,096	(64.0)	12,483	(67.2)	39,507	(61.5)
	Ex-drinker	4,052	(23.9)	3,383	(23.4)	3,255	(22.9)	4,167	(22.4)	14,857	(23.1)
	One to three times/month	2,848	(16.8)	1,806	(12.5)	1,537	(10.8)	1,643	(8.8)	7,834	(12.2)
	Once a week or more	903	(5.3)	484	(3.3)	322	(2.3)	293	(1.6)	2,002	(3.1)
Employed	No	8,820	(52.1)	7,523	(52.0)	7,367	(51.8)	9,861	(53.1)	33,571	(52.3)
	Yes	8,113	(47.9)	6,948	(48.0)	6,843	(48.2)	8,725	(46.9)	30,629	(47.7)
Child sex	Boy	8,344	(49.3)	7,115	(49.2)	6,878	(48.4)	9,129	(49.1)	31,466	(49.0)
	Girl	8,589	(50.7)	7,356	(50.8)	7,332	(51.6)	9,457	(50.9)	32,734	(51.0)
Nursery	No	6,001	(35.4)	5,282	(36.5)	5,138	(36.2)	6,995	(37.6)	23,416	(36.5)
	Yes	10,932	(64.6)	9,189	(63.5)	9,072	(63.8)	11,591	(62.4)	40,784	(63.5)
Location where the baby sleeps at night	In the parent's bed	14,328	(84.6)	12,324	(85.2)	11,984	(84.3)	15,329	(82.5)	53,965	(84.1)
	In a baby bed located in the parent's room	2,345	(13.9)	1,966	(13.6)	2,048	(14.4)	3,013	(16.2)	9,372	(14.6)
	In a baby bed located in a room other than the bedroom of his/her parents	183	(1.1)	137	(1.0)	132	(0.9)	179	(1.0)	631	(1.0)
	Other	77	(0.5)	44	(0.3)	46	(0.3)	65	(0.4)	232	(0.4)
Birth weight, g		3,024		3,034		3,031		3,028		3,029	
Gestational weeks		39.3		39.3		39.3		39.3		39.3	
Eating dairy products	Yes	16,429	(97.0)	14,125	(97.6)	13,884	(97.7)	18,152	(97.7)	62,590	(97.5)
	No	504	(3.0)	346	(2.4)	326	(2.3)	434	(2.3)	1,610	(2.5)
Disease	No	10,026	(59.2)	8,572	(59.2)	8,485	(59.7)	10,973	(59.0)	38,056	(59.3)
	Yes	6,907	(40.8)	5,899	(40.8)	5,725	(40.3)	7,613	(41.0)	26,144	(40.7)
Birth month	1	1,392	(8.2)	1,149	(7.9)	1,055	(7.4)	1,331	(7.2)	4,927	(7.7)
	2	1,222	(7.2)	1,045	(7.2)	944	(6.6)	1,221	(6.6)	4,432	(6.9)
	3	1,395	(8.2)	1,125	(7.8)	1,060	(7.5)	1,330	(7.2)	4,910	(7.6)
	4	1,272	(7.5)	1,121	(7.8)	1,106	(7.8)	1,454	(7.8)	4,953	(7.7)
	5	1,320	(7.8)	1,093	(7.6)	1,170	(8.2)	1,597	(8.6)	5,180	(8.1)
	6	1,141	(6.7)	1,096	(7.6)	1,189	(8.4)	1,645	(8.9)	5,071	(7.9)
	7	1,334	(7.9)	1,287	(8.9)	1,335	(9.4)	1,801	(9.7)	5,757	(9.0)
	8	1,668	(9.9)	1,455	(10.1)	1,445	(10.2)	1,934	(10.4)	6,502	(10.1)
	9	1,715	(10.1)	1,462	(10.1)	1,475	(10.4)	1,915	(10.3)	6,567	(10.2)
	10	1,663	(9.8)	1,398	(9.7)	1,268	(8.9)	1,718	(9.2)	6,047	(9.4)
	11	1,389	(8.2)	1,114	(7.7)	1,091	(7.7)	1,362	(7.3)	4,956	(7.7)
	12	1,422	(8.4)	1,126	(7.8)	1,072	(7.5)	1,278	(6.9)	4,898	(7.6)

BMI; body mass index. JPY; Japanese Yen.

Table 4. Characteristics according to quartile for natto intake during pregnancy in women (N = 64,200).

		Quartile of natto intake									
		1 (low)		2		3		4 (high)		Total	
Median intake of natto, g/day		0		3.3		10.7		25			
Mean intake of energy, cal		1,580		1,587		1,738		1,997		1,736	
Age at delivery, years		31.3		31.2		31.7		32.2		31.6	
Previous deliveries	Nullipara	5,238	(45.6)	6,705	(43.8)	8,865	(40.1)	6,210	(40.6)	27,018	(42.1)
	Multipara	6,239	(54.4)	8,588	(56.2)	13,249	(59.9)	9,106	(59.5)	37182	(57.9)
BMI (kg/m^2)	<18.5	596	(5.2)	693	(4.5)	1,109	(5.0)	820	(5.4)	3,218	(5.0)
	18.5-<25	9,025	(78.6)	12,262	(80.2)	17,844	(80.7)	12,303	(80.3)	51,434	(80.1)
	≥25	1,856	(16.2)	2,338	(15.3)	3,161	(14.3)	2,193	(14.3)	9,548	(14.9)
Highest educational level	Junior high school or high school	3,898	(34.0)	5,187	(33.9)	6,946	(31.4)	4,559	(29.8)	20,590	(32.1)
	Technical junior college, technical/vocational college or associate degree	4,934	(43.0)	6,605	(43.2)	9,675	(43.8)	6,804	(44.4)	28,018	(43.6)
	Bachelor's degree, postgraduate degree	2,645	(23.1)	3,501	(22.9)	5,493	(24.8)	3,953	(25.8)	15,592	(24.3)
Annual household income, JPY	<4 million	4,707	(41.0)	6,049	(39.6)	8,175	(37.0)	5,566	(36.3)	24,497	(38.2)
	4-6 million	3,764	(32.8)	5,153	(33.7)	7,623	(34.5)	5,246	(34.3)	21,786	(33.9)
	>6 million	3,006	(26.2)	4,091	(26.8)	6,316	(28.6)	4,504	(29.4)	17,917	(27.9)
Marital status	Married (including common law marriage)	11,276	(98.3)	15,074	(98.6)	21,845	(98.8)	15,157	(99.0)	63,352	(98.7)
	Divorced or widowed	98	(0.9)	107	(0.7)	132	(0.6)	68	(0.4)	405	(0.6)
	Others	103	(0.9)	112	(0.7)	137	(0.6)	91	(0.6)	443	(0.7)
Alcohol intake, 1m	Never	10,591	(92.3)	14,009	(91.6)	20,259	(91.6)	14,095	(92.0)	58,954	(91.8)
	Ex-drinekr	510	(4.4)	668	(4.4)	994	(4.5)	629	(4.1)	2,801	(4.4)
	One to three times/month	254	(2.2)	424	(2.8)	602	(2.7)	408	(2.7)	1,688	(2.6)
	Once a week or more	122	(1.1)	192	(1.3)	259	(1.2)	184	(1.2)	757	(1.2)
Smoking status, 1m	Never	7,167	(62.5)	9,173	(60.0)	13,580	(61.4)	9,587	(62.6)	39,507	(61.5)
	Ex-drinekr	2,324	(20.3)	3,491	(22.8)	5,305	(24.0)	3,737	(24.4)	14,857	(23.1)
	One to three times/month	1,498	(13.1)	2,076	(13.6)	2,586	(11.7)	1,674	(10.9)	7,834	(12.2)
	Once a week or more	488	(4.3)	553	(3.6)	643	(2.9)	318	(2.1)	2,002	(3.1)
Employed, 1y	No	5,911	(51.5)	7,815	(51.1)	11,618	(52.5)	8,227	(53.7)	33,571	(52.3)
	Yes	5,566	(48.5)	7,478	(48.9)	10,496	(47.5)	7,089	(46.3)	30,629	(47.7)
Child sex	Boy	5,593	(48.7)	7,597	(49.7)	10,837	(49.0)	7,439	(48.6)	31,466	(49.0)
	Girl	5,884	(51.3)	7,696	(50.3)	11,277	(51.0)	7,877	(51.4)	32,734	(51.0)
Nursery, 3y	No	3,918	(34.1)	5,360	(35.1)	8,144	(36.8)	5,994	(39.1)	23,416	(36.5)
	Yes	7,559	(65.9)	9,933	(65.0)	13,970	(63.2)	9,322	(60.9)	40,784	(63.5)
Location where the baby sleeps at night, 3y	In the parent's bed	9,478	(82.6)	12,853	(84.0)	18,783	(84.9)	12,851	(83.9)	53,965	(84.1)
	In a baby bed located in the parent's room	1,829	(15.9)	2,216	(14.5)	3,066	(13.9)	2,261	(14.8)	9,372	(14.6)
	In a baby bed located in a room other than the bedroom of his/her parents	128	(1.1)	177	(1.2)	189	(0.9)	137	(0.9)	631	(1.0)
	Other	42	(0.4)	47	(0.3)	76	(0.3)	67	(0.4)	232	(0.4)
Birth weight, g			3,011		3,025		3,037		3,035		3,029
Gestational weeks			39.3		39.3		39.3		39.3		39.3
Eating dairy products, 3y	Yes	11,166	(97.3)	14,910	(97.5)	21,595	(97.7)	14,919	(97.4)	62,590	(97.5)
	No	311	(2.7)	383	(2.5)	519	(2.4)	397	(2.6)	1,610	(2.5)
Disease, 3y	No	6,892	(60.1)	9,062	(59.3)	13,077	(59.1)	9,025	(58.9)	38,056	(59.3)
	Yes	4,585	(40.0)	6,231	(40.7)	9,037	(40.9)	6,291	(41.1)	26,144	(40.7)
Birth month	1	857	(7.5)	1,234	(8.1)	1,709	(7.7)	1,127	(7.4)	4,927	(7.7)
	2	855	(7.5)	1,075	(7.0)	1,498	(6.8)	1,004	(6.6)	4,432	(6.9)
	3	891	(7.8)	1,198	(7.8)	1,616	(7.3)	1,205	(7.9)	4,910	(7.6)
	4	901	(7.9)	1,135	(7.4)	1,693	(7.7)	1,224	(8.0)	4,953	(7.7)
	5	866	(7.6)	1,183	(7.7)	1,835	(8.3)	1,296	(8.5)	5,180	(8.1)
	6	826	(7.2)	1,093	(7.2)	1,803	(8.2)	1,349	(8.8)	5,071	(7.9)
	7	994	(8.7)	1,305	(8.5)	2,035	(9.2)	1,423	(9.3)	5,757	(9.0)
	8	1,125	(9.8)	1,528	(10.0)	2,281	(10.3)	1,568	(10.2)	6,502	(10.1)
	9	1,178	(10.3)	1,603	(10.5)	2,230	(10.1)	1,556	(10.2)	6,567	(10.2)
	10	1,135	(9.9)	1,500	(9.8)	2,028	(9.2)	1,384	(9.0)	6,047	(9.4)
	11	933	(8.1)	1,178	(7.7)	1,755	(7.9)	1,090	(7.1)	4,956	(7.7)
	12	916	(8.0)	1,261	(8.3)	1,631	(7.4)	1,090	(7.1)	4,898	(7.6)

BMI; body mass index. JPY; Japanese Yen.

ORs for children not meeting the 10-h sleep duration target were evaluated based on intake of miso, yogurt, cheese, and natto. In the cheese evaluation, ORs for inadequate sleep duration were significantly lower for children with mothers in the highest quartile of intake, and these associations were significant according to a trend test (Table 5).

In additional analyses, ORs were calculated for overall fermented food intake and children's sleep duration. The results showed that the OR for inadequate sleep duration was significantly lower for children whose mothers were in the highest quartile (adjusted OR 0.90, 95% CI 0.82–0.99), but not in the second (adjusted OR 0.99, 95% CI 0.91–1.08) or third (adjusted OR 0.94, 95% CI 0.87–1.03) quartile.

Table 5. Odds ratios (95% confidence intervals) for 3-year-old infants for risk of sleeping less than 10 hours according to quartile for maternal intake of fermented food during pregnancy (N = 64,200).

	Quartiles for fermented food intake				*p*-value
	1 (low)	2	3	4 (high)	for trend
Median intake of miso, g/day	10.0	32.1	88.4	225.0	
Total, n	16,401	13,720	17,988	16,091	
Cases, n	1,238	943	1,279	1,219	
Crude odds ratio	1.00 (Ref.)	0.90 (0.83–0.99)	0.94 (0.86–1.02)	1.00 (0.93–1.09)	0.809
Adjusted odds ratio	1.00 (Ref.)	0.91 (0.84–1.00)	0.95 (0.87–1.03)	1.00 (0.92–1.09)	0.863
Median intake of yogurt, g/day	8.0	25.7	60.0	120.0	
Total, n	16,933	14,471	14,210	18,586	
Cases, n	1,236	1,064	1,042	1,337	
Crude odds ratio	1.00 (Ref.)	1.01 (0.93–1.10)	1.01 (0.92–1.10)	0.98 (0.91–1.07)	0.689
Adjusted odds ratio	1.00 (Ref.)	1.04 (0.95–1.13)	1.04 (0.95–1.14)	1.02 (0.94–1.11)	0.674
Median intake of cheese, g/day	0.0	1.3	4.3	10.0	
Total, n	15,404	16,357	16,912	15,527	
Cases, n	1,190	1,231	1,212	1,046	
Crude odds ratio	1.00 (Ref.)	0.97 (0.90–1.06)	0.92 (0.85–1.00)	**0.86 (0.79–0.94)**	**<0.001**
Adjusted odds ratio	1.00 (Ref.)	0.98 (0.90–1.06)	0.93 (0.85–1.01)	**0.85 (0.78–0.94)**	**<0.001**
Median intake of natto, g/day	0.0	3.3	10.7	25.0	
Total, n	11,477	15,293	22,114	15,316	
Cases, n	869	1,151	1,557	1,102	
Crude odds ratio	1.00 (Ref.)	0.99 (0.91–1.09)	0.93 (0.85–1.01)	0.95 (0.86–1.04)	0.089
Adjusted odds ratio	1.00 (Ref.)	1.00 (0.91–1.10)	0.93 (0.86–1.02)	0.95 (0.86–1.05)	0.133

Bold indicates significance.

Adjusted for were energy intake, maternal age during pregnancy, previous deliveries during pregnancy, body mass index (BMI) at 1 month after delivery, highest maternal educational level, annual household income, marital status at 6 months after delivery, alcohol intake at 1 month after delivery, smoking status at 1 month after delivery, employment status at 1 year after delivery, child sex, infant attendance at nursery (at 1 year of age), the location where the infant slept at night (at 1 year of age), birth weight, gestational period, eating dairy products at 3 years of age, presence of any disease (up to 3 years of age), and date (month) of birth.

Discussion

This study used data from 64,200 mother-child pairs from the JECS to determine the association of the dietary intake of fermented foods during pregnancy with less than 10 h of sleep among 3-year-old children. The results showed that cheese intake during pregnancy was associated with a significantly lower risk of sleep deprivation (< 10 h) among children of mothers in the fourth quartile compared with children of mothers in the first quartile. Miso intake was found to be associated with sleep duration in 1-year-old children [16] but not in 3-year-old children. These findings suggest that the effect of mothers' consumption of fermented foods during pregnancy on their children's sleep can continue to at least at 3 years of age.

The current results on the association between the maternal consumption of fermented foods during pregnancy and sleep duration in 3-year-old children are consistent with those from previous studies. It has already been reported that fermented foods positively affect the intestinal bacterial activity and growth [36].

In a randomized controlled trial with human participants, a group that consumed fermented foods such as yogurt and kimchi for 10 weeks had a greater variety of intestinal bacteria 4 weeks after the end of the study [37]. Animal experiments have shown that the gut microbiota, in addition to changing sleep-wake patterns and sleep quality, significantly alters gut metabolism, that the gut microbiota has a circadian rhythm, and that the intestinal bacteria exhibit circadian rhythms in composition and activity [38, 39]. It was also shown that mice without gut microbes have disrupted circadian rhythms compared with those with gut microbes [40]. In addition, maternal melatonin affects the fetus through the placenta [41, 42], and the gut microbiota is transferred to the infant at birth, causing changes in the infant's gut microbiota [15]. The intestinal microbiota also reflects significant metabolic changes in the intestinal tract as well as changes in sleep-wake patterns and sleep quality [13]. Intestinal bacteria and hormones are thus expected to be closely related to sleep. Accordingly, fermented foods, intestinal flora, and hormones are closely related to sleep and the mother's gut microbiota may have long-term effects on the child after birth.

The main strength of my study was the large sample size of over 60,000 mother–child pairs and the fact that the sample can be considered representative of mothers and toddlers in Japan, given that the JECS covers a wide geographic range across 15 regions. However, this study also has some limitations. Similar to the previous study [16], I did not directly investigate changes in intestinal microbiota. Another limitation is the reliance on maternal reports of child sleep duration. I observed that pregnant women who were well-educated and employed, and had higher income tended to have higher fermented food intake. To explain this, I speculated that these women likely recognized factors contributing to health and therefore tended to choose nutrient-rich options, such as fermented foods, more frequently than nutritionally unbalanced and/or nutrient-deficient options, such as junk food. The women's health consciousness might affect the sleep duration of their children. In fact, the study found that cheese intake was associated with "health consciousness" factors such as BMI, education level, household income, and smoking status. Although I adjusted for these factors, "health consciousness" remained as a hidden factor independent of these other factors.

Conclusion

In this study, 64,200 pairs of mothers and their children were surveyed to determine the association between the mothers' intake of fermented foods during pregnancy and their children's sleep duration at 3 years of age. The results showed that mothers who consumed more cheese during pregnancy had a reduced risk of their children sleeping less than 10 h per night.

Second division

Dietary intake of yogurt and cheese in children at age 1 year and sleep duration at age 1 and 3 years: the Japan Environment and Children's Study

Abstract

Background: Sugimori et al previously reported that 1-year-old infants born to mothers who regularly consumed fermented food during pregnancy had a lower risk of sleep deprivation. However, it is not known if these positive effects are enhanced when infants themselves eat fermented foods or the long-term effects of such consumption. In this study, I examined the association between the frequency of fermented food intake during the child's weaning period and sleep deprivation at age 1 and 3 years.

Methods: This birth cohort study used data from a nationwide, government-funded study called the Japan Environment and Children's Study (JECS), covering 65,210 mother-child pairs. I examined the association between infants' consumption of fermented foods at 1 year of age and sleep deprivation at 1 and 3 years of age.

Results: There was no association between yogurt or cheese intake and sleep duration at age 1; at age 3, there was no between-group difference, although a trend test showed that yogurt intake at age 1 was significantly associated with sleep duration at age 3. There was also no association between the frequency of cheese intake and inadequate sleep duration at age 3.

Conclusions: Frequency of children's yogurt and cheese intake at age 1 was not associated with sleep duration at age 1 or 3. However, a trend test showed a significant association between the frequency of yogurt intake at age 1 and sleep duration at age 3.

Keywords: Birth cohort, Sleep, Fermented foods

Background

A sufficient amount of good sleep is necessary for a healthy life. Lack of sleep and irregular sleep patterns have been reported to increase the risk of physical illnesses [43], such as hypertension [44] and diabetes [45], and mental illnesses, such as depression [46, 47] and self-harm [48]. This is true not only for adults but also children, whose sleep duration varies from the neonatal period to infancy [2]. Sleep deprivation in infancy has been found to be associated with obesity [20], poor academic and spatial skills [49], hyperactivity [19], problematic behavior [50], and hyperactivity at age 6 years [20], and it has a negative impact on physical and psychological development. It is therefore important to investigate the causes and effects of sleep deprivation in infancy.

Probiotic-containing foods and fermented foods are gaining attention due to their positive effects on the gut microbiota [11, 12], and a good gut microbiota has a positive effect on sleep [13, 14]. Studies on probiotic-containing foods and/or the gut microbiota include a small study of 8 people in which consumption of yogurt-containing probiotics improved gut bacteria after antibiotic treatment [51]. In a study of 66 elderly people, a probiotic group treated daily for 6 months with a fermented flavored oat drink containing 109 cfu/mL Bifidobacterium longum 46 (DSM 14583) and B. longum 2C (DSM 14579) also showed higher and more diverse levels of bifidobacteria in their stool [52]. Interestingly, in a study of the gut microbiota and sleep in 37 healthy elderly people, a higher proportion of Verrucomicrobia and Lentisphaerae in their stool was associated with better sleep quality and better Stroop performance [53]. A study of 9 men determined that a sleep-deprived group, which slept about 4 h, had lower total amounts of acetate, propionate, and fecal short-chain fatty acids in their stool, suggesting the importance of sleep duration and the composition of the gut microbiota [54]. Furthermore, a study of 40 men also reported that diversity of the microbiome in the gut microbiota was positively correlated with sleep efficiency and total sleep time and was negatively correlated with sleep fragmentation [55].

However, as yet, there is a lack of research involving children, particularly infants, a lack of large-scale studies, and a lack of research focusing directly on sleep from the perspective of dietary content.

The Japan Environment and Children's Study (JECS), known as Ecochil-Chosa in Japan, is a nationwide birth cohort study investigating the environmental factors possibly affecting children's health and development. A total of 104,059 pregnancies have been registered, and data from self-administered questionnaires and medical record transcriptions have yielded a wide array of research findings [56]. The JECS previously examined the association between the frequency of the maternal consumption of fermented foods during pregnancy and the infant's sleep duration at 1 year of age in 72,624 mother-infant pairs [16]. Infants whose mothers consumed miso soup more often during pregnancy were found to sleep longer. Similar results were obtained for cheese and sleep at age 3 [17]. These results suggest that a high intake of fermented foods during pregnancy may have a positive effect on the child's sleep. However, it is also conceivable that the child's diet may have a greater impact on their development than the mother's diet during pregnancy.

In this study, I focused on yogurt and cheese, which are often consumed in Japan as probiotic-containing fermented foods, and examined the association between frequency of intake at age 1 and sleep duration at ages 1 and 3.

Methods

Study population

The JECS protocol has been described in detail elsewhere [30, 31]. Briefly, the aim of the JECS, a nationwide government-funded birth cohort study, is to determine the impact of certain environmental factors on child health and development. The JECS participants included women in the first trimester of pregnancy, belonging to 15 regions of Japan, who were enrolled between January 2011 and March 2014 [30, 31]. The eligibility criteria for participants (expectant mothers) were as follows: 1) resident of a Study Area at the time of recruitment and expected to reside continually in Japan for the foreseeable future; 2) expected delivery date between August 1, 2011, and mid-2014; and 3) able to participate in the study without difficulty (i.e., able to understand Japanese and complete the self-administered questionnaire). The excluded participants were expectant mothers residing outside the Study Area, even if they visited co-operating health care providers within a Study Area. The present study analyzed the jecs-qa-20210401 (jecs-ta-20190930) dataset, released in April 2021. The full dataset comprises 104,059 records obtained from a questionnaire-based survey of the participants. I excluded 3,759 and 1,891 records because of miscarriages/still births and multiple births, respectively (Figure. 1). Additionally, I excluded 20,204 participants with missing data on sleep duration and 957 participants with missing data on yogurt or cheese consumption.

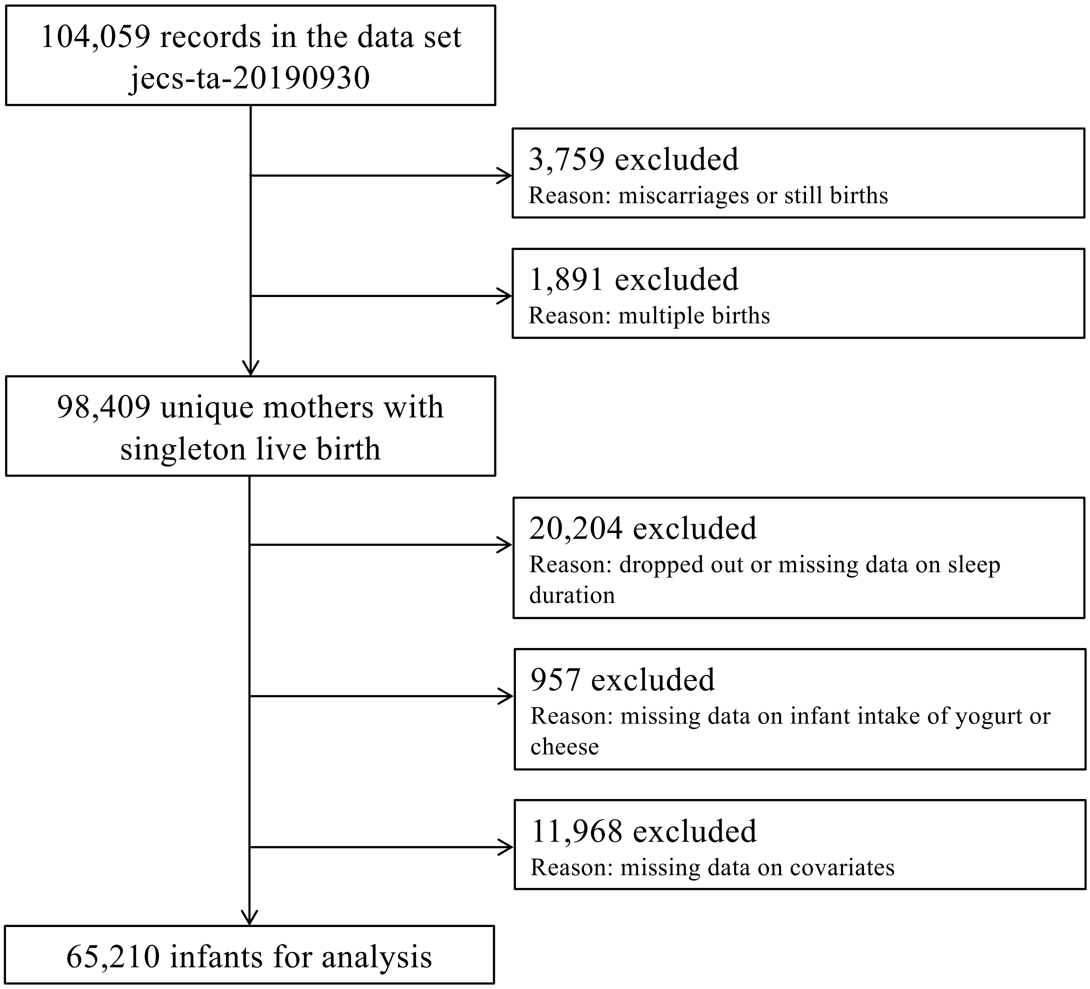

Figure. 1 Flow diagram of the recruitment and exclusion process for participants

Data assessment

Exposure

To assess the frequency of probiotic intake, the following questions were included in a self-administered questionnaire that mothers completed 1 year after delivery: "How many times a week does your child have yogurt?" and "How many times a week does your child have cheese?" The response options were < 1 time/week, 1–2 days/week, 3–4 days/week, 5–6 days/week, 1 time/day, 2 times/day, and ≥ 3 times/day. Because of variation in the number of responses in the frequency categories for yogurt and cheese, categorization was performed by food. Specifically, I categorized participant responses for the consumption of yogurt by infants as < 1 time/week, 1–2 days/week, 3–6 days/week, or ≥ 7 times/week and for cheese as < 1 time/week, 1–2 times/week, or ≥ 3 times/week [34].

Outcome categories

To measure infant sleep duration at 1 and 3 years after delivery, parents were asked in the questionnaire to indicate when their infant slept on the previous day. Parents marked the times when their infant was asleep by drawing lines through boxes indicating 30-min intervals from 12:00 am to 12:00 am the next day [16]. Infants were categorized according to tertile or quartile of fermented food intake to estimate their risk of sleep deprivation. The National Sleep Foundation in the United States recommends 11–14 h of sleep in a 24-h period for 1-year-olds and 10–13 h for 3-year-olds. Therefore, the lower limit of appropriate sleep duration was set at less than 11 h for 1-year-olds and 10 h for 3-year-olds [2].

Confounders in multiple logistic regression analysis

The following confounding factors were used in multiple logistic regression: maternal age; body mass index (kg/m2) 1 month after delivery (< 18.5, 18.5–25, or ≥ 25); number of previous deliveries (nulliparous or multiparous); educational background (junior high school or high school, technical junior college, technical/vocational college or associate degree, or Bachelor's degree or postgraduate degree); annual household income (< 4 million JPY, 4–6 million JPY, or ≥ 6 million JPY); marriage status 6 months after delivery (married, divorced, widowed, or other); alcohol status 1 month after delivery (never, ex-drinker, 1–3 times/month, 1–3 times/week, 4–6 times/week, or every day); smoking status 1 month after delivery (never, quit before learning of pregnancy, quit after learning of pregnancy, currently smoking (≤ 10 cigarettes or ≥ 10 cigarettes); employment status 1 year after delivery (employed or unemployed); cesarean section (no or yes); gestational age at birth (weeks); birth weight (g); infant sex (male or female); major congenital anomaly (no or yes); birth season (spring, summer, fall, or winter), night crying at 1 year of age (no or yes); and attending nursery school at 1 year of age (no or yes). These variables were categorized according to standard medical practice or common practice in Japan [33, 57] and as shown in Tables 1, 2, and 3.

Statistical analysis

Unless stated otherwise, data are expressed as mean ± standard deviation or median. Univariate and multivariate logistic analyses were applied to estimate the incidence of inadequate sleep duration (< 11 h at 1 year of age and < 10 h at 3 years of age). Four logistic analyses were conducted to determine the association between the frequency of yogurt intake at age 1 and sleep at age 1, frequency of yogurt intake at age 1 and sleep at age 3, frequency of cheese intake at age 1 and sleep at age 1, and frequency of cheese intake at age 1 and sleep at age 3[17]. I calculated both unadjusted and adjusted odds ratios (ORs) with 95% confidence intervals (95% CIs).

ORs and 95% CIs were calculated using logistic regression analysis with yogurt as the lowest quartile criterion and cheese as the lowest tertile criterion. Adjusted ORs were calculated using the covariates described in the previous section, and crude ORs were calculated without these covariates. The JECS prohibits the sharing of the ORs of covariates, regardless of whether they are crude or adjusted. Trend tests were conducted with yogurt and cheese intake respectively assessed using quartile and tertile distributions as continuous variables. All statistical analyses were performed by using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Ethics approval and consent to participate

The JECS comprehensive protocol 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. All participants provided written informed consent. This specific study was approved by the Ethics Committee of the University of Toyama (R2018032). The JECS is conducted in accordance with the Helsinki Declaration and other national regulations, and written informed consent was obtained from the parents/guardians of participants under 16 years of age.

Results

Demographic and obstetric characteristics of participants (n = 65,210) are shown in Tables 1 and 2. The group with higher yogurt consumption was more likely to be primiparous, to have a higher household income, and not to attend nursery school. On the other hand, the group that consumed more cheese tended to be primiparous and more educated and to have a higher household income; in addition, the mothers tended to be unemployed and the infants tended to not attend nursery school.

Table 1. Participant characteristics by frequency of infant consumption of yogurt at 1 year of age

	Yogurt consumption at 1 year of age, times/week							
	< 1 (n = 13,443)		1–2 (n = 20,612)		3–6 (n = 19,811)		≥ 7 (n = 11,344)	
	n	(%)	n	(%)	n	(%)	n	(%)
Mother's age at childbirth								
Mean ± SD, y	31.6 ± 4.81		31.3 ± 4.83		31.6 ± 4.77		32.1 ± 4.75	
Pre-pregnancy BMI, kg/m^2								
< 18.5	701	(5.2)	905	(4.4)	1,002	(5.1)	662	(5.8)
18.5 to < 25	10,770	(80.1)	16,409	(79.6)	15,968	(80.6)	9,053	(79.8)
≥ 25	1,972	(14.7)	3,298	(16.0)	2,841	(14.3)	1,629	(14.4)
Parity								
Primiparous	4,720	(35.1)	7,256	(35.2)	8,989	(45.4)	6,374	(56.2)
Multiparous	8,723	(64.9)	13,356	(64.8)	10,822	(54.6)	4,970	(43.8)
Highest education level, y								
≤ 12	4,392	(32.7)	7,283	(35.3)	6,036	(30.5)	3,202	(28.2)
12 to < 16	5,641	(42.0)	8,826	(42.8)	8,824	(44.5)	5,092	(44.9)
≥ 16	3,410	(25.4)	4,503	(21.9)	4,951	(25.0)	3,050	(26.9)
Annual household income, JPY								
< 4 million	5,416	(40.3)	8,399	(40.8)	7,189	(36.3)	3,794	(33.4)
4 to < 6 million	4,533	(33.7)	6,981	(33.9)	6,788	(34.3)	3,792	(33.4)
≥ 6 million	3,494	(26.0)	5,232	(25.4)	5,834	(29.5)	3,758	(33.1)
Marital status								
Married	13,262	(98.7)	20,317	(98.6)	19,580	(98.8)	11,195	(98.7)
Divorced or widowed	181	(1.4)	295	(1.4)	231	(1.2)	149	(1.3)
Alcohol intake								
Never	12,323	(91.7)	18,761	(91.0)	18,251	(92.1)	10,550	(93.0)
Former	563	(4.2)	944	(4.6)	870	(4.4)	467	(4.1)
Current	557	(4.1)	907	(4.4)	690	(3.5)	327	(2.9)
Smoking history								
Never	8,241	(61.3)	12,195	(59.2)	12,324	(62.2)	7,327	(64.6)
Quit	4,764	(35.4)	7,645	(37.1)	6,930	(35.0)	3,767	(33.2)
Current	438	(3.3)	772	(3.8)	557	(2.8)	250	(2.2)
Employed								
No	7,272	(54.1)	10,210	(49.5)	10,164	(51.3)	6,179	(54.5)
Yes	6,171	(45.9)	10,402	(50.5)	9,647	(48.7)	5,165	(45.5)
Cesarean section								
No	10,928	(81.3)	16,989	(82.4)	16,170	(81.6)	9,129	(80.5)
Yes	2,515	(18.7)	3,623	(17.6)	3,641	(18.4)	2,215	(19.5)
Gestational weeks								
Mean ± SD, weeks	39.3 ± 1.55		39.3 ± 1.44		39.3 ± 1.46		39.3 ± 1.47	
Birth weight								
Mean ± SD, kg	3035 ± 413.5		3036 ± 402.9		3028 ± 402.9		3016 ± 403.5	
Infant sex								
Male	6,987	(52.0)	10,324	(50.1)	10,048	(50.7)	5,922	(52.2)
Female	6,456	(48.0)	10,288	(49.9)	9,763	(49.3)	5,422	(47.8)
Major congenital anomaly								
No	13,150	(97.8)	20,176	(97.9)	19,364	(97.7)	11,074	(97.6)
Yes	293	(2.2)	436	(2.1)	447	(2.3)	270	(2.4)
Birth season								
Spring (months 3–5)	3,000	(22.3)	4,782	(23.2)	4,756	(24.0)	2,731	(24.1)
Summer (months 6–8)	3,381	(25.2)	5,551	(26.9)	5,488	(27.7)	3,228	(28.5)
Fall (months 9–11)	3,856	(28.7)	5,664	(27.5)	5,341	(27.0)	2,969	(26.2)
Winter (months 12–2)	3,206	(23.9)	4,615	(22.4)	4,226	(21.3)	2,416	(21.3)
Night crying at 1 year of age								
No	6,827	(50.8)	10,679	(51.8)	10,150	(51.2)	5,883	(51.9)
Yes	6,616	(49.2)	9,933	(48.2)	9,661	(48.8)	5,461	(48.1)
Nursery attendance at 1 year of age								
No	9,874	(73.5)	14,157	(68.7)	14,727	(74.3)	9,094	(80.2)
Yes	3,569	(26.6)	6,455	(31.3)	5,084	(25.7)	2,250	(19.8)

BMI; body mass index. JPY; Japanese Yen.

Table 2. Participant characteristics by frequency of infant consumption of cheese at 1 year of age

	Cheese consumption at 1 year of age, times/week					
	<1 (n = 30,614)		1–2 (n = 26,178)		≥ 3 (n = 8,418)	
	n	(%)	n	(%)	n	(%)
Mother's age at childbirth						
Mean ± SD, y	31.6 ± 4.79		31.5 ± 4.82		32.0 ± 4.75	
Pre-pregnancy BMI, kg/m^2						
< 18.5	1,592	(5.2)	1,218	(4.7)	460	(5.5)
18.5 to < 25	24,373	(79.6)	21,050	(80.4)	6,777	(80.5)
≥ 25	4,649	(15.2)	3,910	(14.9)	1,181	(14.0)
Parity						
Primiparous	12,277	(40.1)	10,933	(41.8)	4,129	(49.1)
Multiparous	18,337	(59.9)	15,245	(58.2)	4,289	(51.0)
Highest education level, y						
≤ 12	9,974	(32.6)	8,650	(33.0)	2,289	(27.2)
12 to < 16	13,248	(43.3)	11,393	(43.5)	3,742	(44.5)
≥ 16	7,392	(24.2)	6,135	(23.4)	2,387	(28.4)
Annual household income, JPY						
< 4 million	12,044	(39.3)	9,833	(37.6)	2,921	(34.7)
4 to < 6 million	10,266	(33.5)	8,929	(34.1)	2,899	(34.4)
≥ 6 million	8,304	(27.1)	7,416	(28.3)	2,598	(30.9)
Marital status						
Married	30,229	(98.7)	25,809	(98.6)	8,316	(98.8)
Divorced or widowed	385	(1.3)	369	(1.4)	102	(1.2)
Alcohol intake						
Never	28,337	(92.6)	23,831	(91.0)	7,717	(91.7)
Former	1,238	(4.0)	1,198	(4.6)	408	(4.9)
Current	1,039	(3.4)	1,149	(4.4)	293	(3.5)
Smoking history						
Never	19,205	(62.7)	15,622	(59.7)	5,260	(62.5)
Quit	10,489	(34.3)	9,645	(36.8)	2,972	(35.3)
Current	920	(3.0)	911	(3.5)	186	(2.2)
Employed						
No	15,911	(52.0)	13,175	(50.3)	4,739	(56.3)
Yes	14,703	(48.0)	13,003	(49.7)	3,679	(43.7)
Cesarean section						
No	24,943	(81.5)	21,365	(81.6)	6,908	(82.1)
Yes	5,671	(18.5)	4,813	(18.4)	1,510	(17.9)
Gestational weeks						
Mean ± SD, weeks	39.2 ± 1.56		39.3 ± 1.41		39.3 ± 1.36	
Birth weight						
Mean ± SD, kg	3029 ± 415.7		3032 ± 399.1		3028 ± 385.6	
Infant sex						
Male	15,646	(51.1)	13,319	(50.9)	4,316	(51.3)
Female	14,968	(48.9)	12,859	(49.1)	4,102	(48.7)
Major congenital anomaly						
No	29,913	(97.7)	25,625	(97.9)	8,226	(97.7)
Yes	701	(2.3)	553	(2.1)	192	(2.3)
Birth season						
Spring (months 3–5)	6,927	(22.6)	6,332	(24.2)	2,010	(23.9)
Summer (months 6–8)	8,036	(26.3)	7,264	(27.8)	2,348	(27.9)
Fall (months 9–11)	8,655	(28.3)	6,959	(26.6)	2,216	(26.3)
Winter (months 12–2)	6,996	(22.9)	5,623	(21.5)	1,844	(21.9)
Night crying at 1 year of age						
No	15,758	(51.5)	13,492	(51.5)	4,289	(51.0)
Yes	14,856	(48.5)	12,686	(48.5)	4,129	(49.1)
Nursery attendance at 1 year of age						
No	22,601	(73.8)	18,634	(71.2)	6,617	(78.6)
Yes	8,013	(26.2)	7,544	(28.8)	1,801	(21.4)

BMI; body mass index. JPY; Japanese Yen.

The unadjusted and adjusted ORs (95% CIs) for the relationship of inadequate sleep duration with yogurt and cheese consumption at 1 and 3 years of age are shown in Table 3. In terms of frequency of yogurt intake at age 1 and sleep duration at age 3, the incidence of children with sleep deprivation decreased when yogurt was consumed ≥ 7 times per week in the crude model. The adjusted model showed no differences between groups, although a trend test showed significant differences. In all other conditions, there were no significant differences in both the crude and adjusted models.

Table 3. ORs (95% CIs) for inadequate sleep duration at 1 and 3 years of age according to frequency of infant consumption of yogurt and cheese at 1 year of age (n = 65,210)

	Cases, n	Controls, n	Crude model[a] Odds ratios (95% CI)	Adjusted model[a, b] Odds ratios (95% CI)	*p*-value for trend[c]
Sleep deprivation at 1 year of age (cross-sectional design)					
Yogurt, times/week					
< 1	1,261 /	12,182	Reference	Reference	0.793
1–2	1,988 /	18,624	1.031 (0.938–1.133)	1.000 (0.909–1.100)	
3–6	1,766 /	18,045	0.945 (0.858–1.041)	0.939 (0.852–1.035)	
≥ 7	1,022 /	10,322	0.956 (0.857–1.068)	0.974 (0.871–1.090)	
Cheese, times/week					
< 1	2,818 /	27,796	Reference	Reference	3.707
1–2	2,461 /	23,717	1.024 (0.952–1.100)	1.005 (0.935–1.081)	
≥ 3	758 /	7,660	0.976 (0.877–1.087)	1.001 (0.898–1.115)	
Sleep deprivation at 3 years of age (longitudinal design)					
Yogurt, times/week					
< 1	1,038 /	12,405	Reference	Reference	**0.042**
1–2	1,590 /	19,022	0.999 (0.901–1.108)	0.966 (0.870–1.073)	
3–6	1,425 /	18,386	0.926 (0.833–1.030)	0.917 (0.824–1.020)	
≥ 7	779 /	10,565	**0.881 (0.779–0.996)**	0.897 (0.791–1.016)	
Cheese, times/week					
< 1	2,263 /	28,351	Reference	Reference	2.532
1–2	1,935 /	24,243	1.000 (0.923–1.084)	0.979 (0.904–1.062)	
≥ 3	634 /	7,784	1.021 (0.908–1.147)	1.047 (0.930–1.177)	

Bold indicates significance.

[a] 95% CI after application of Bonferroni correction corresponding to the 98.75% (=100 – 5/4) CIs before Bonferroni correction.

[b] Adjusted for maternal age, pre-pregnancy body mass index, parity, highest education level, annual household income, marital status, alcohol intake, smoking history, employed, cesarean section, gestational weeks, birth weight, infant sex, major congenital anomalies, birth season, night cry, nursery.

[c] Values were multiplied by 4 so that the significance level after Bonferroni correction remains at 5%.

Discussion

In this study, I hypothesized that, as newborns grow, they will be influenced by the foods that they eat, and using data from 65,210 infants in the JECS, I examined the association between the frequency of consumption of two fermented foods (yogurt and cheese) at age 1 year and sleep deprivation at age 1 and 3 years. The results showed that there was no association between the frequency of yogurt intake and sleep duration at age 1, and no difference was found among the groups for sleep duration at age 3, although a trend test revealed a difference. On the other hand, no association was found for the frequency of cheese intake at both age 1 and age 3.

Sugimori et al and I have already reported an association between the active maternal intake of fermented foods during pregnancy and a lower incidence of sleep deprivation at age 1 and 3, suggesting that the maternal diet has a relatively long-term effect on child sleep [16, 17]. In addition, in the present study, a trend test showed an association between the frequency of yogurt intake at age 1 and sleep duration at age 3. In other words, I cannot rule out the possibility that children's own active consumption of fermented foods may affect their sleep or the possible influence of what they themselves eat as they grow up. Indeed, it has been reported that the active administration of probiotics diversifies the intestinal microbiota [37], that the intestinal microbiota has a circadian rhythm, and that the intestinal microbiota is necessary for the proper regulation of the circadian rhythms [38-40]. Moreover, animal studies have shown that the gut microbiota also affects the sleep-wake cycle, a basic state transition of the brain, and that abnormalities in the gut microbiota can lead to disturbances in brain functions such as memory formation, cognitive function, mental health, and circadian rhythms. Analysis of sleep-wake states by electroencephalography and electromyography has revealed that non-REM sleep during the sleep phase is decreased in mice in which the gut microbiota was removed and, conversely, that non-REM and REM sleep during the active phase are increased compared with normal mice [11].

This study analyzed a large dataset from participants who were considered to be representative of the Japanese population [31]. The strength of the study is that it was able to adjust for a large number of covariates. On the other hand, some limitations also exist and may be related to why the hypotheses of this study were not supported. First, the questionnaire used in this study may have been affected by the fact that it did not take into account the type of yogurt or cheese consumed. In particular, there are two types of cheese: natural cheese, which contains live lactic acid bacteria and enzymes, and processed cheese, in which the lactic acid bacteria are killed by heat treatment during cheese production. This raises the question of whether the cheese consumed was actually probiotic. Probiotic cow cheese causes changes in the intestinal microbiota of mice and supports them by delivering probiotic bacteria to their intestines [58], suggesting that the type of cheese a child eats may also be important. Future studies should use methods to compare probiotic preparations containing different concentrations of microorganisms. Second, the questionnaire used in this study asked about the frequency of consumption, not the amount consumed. Further work is needed to determine the exact amount of probiotics actually consumed and changes in the intestinal microbiota by direct investigation. Third, sleep duration was measured at age 1 and at age 3; sleep duration at age 2 is not known. In other words, changes in children's sleep duration were not captured. Fourth, for yogurt and cheese, only the frequency of intake at age 1 was studied, and changes up to age 3 were not ascertained. In particular, the frequency of cheese intake at age 1 was generally lower and more deficient than that of yogurt. Further research is needed to examine the relationship between sleep and the active intake of fermented foods after the age of 1 year and over a longer period of time. Future research should improve on these limitations and long-term studies should examine the relationship between children's diet and sleep duration.

Conclusion

The frequency of children's yogurt and cheese intake at age 1 was not associated with sleep duration at age 1 or 3. However, a trend test showed a significant association between the frequency of yogurt intake at age 1 and sleep duration at age 3.

Conclusions

The purpose of this study was to clarify the relationship between the intake of fermented foods and sleep duration in children through two studies. The results showed that mothers who consumed more cheese during pregnancy had a reduced risk of their children sleeping less than 10 hours at age of 3 years. I studied the association between children's own intake of fermented foods at age 1 year and the risk of sleep deprivation at age 1 and 3 years, respectively, in 65,210 and 52,210 children. The results showed that the frequency of yogurt consumption at age 1 was significantly different from the risk of their children sleeping less than 10 hours at age 3 by a trend test, but there were no differences among the counties. The results of my this study suggest that active consumption of fermented foods by pregnant mothers and children themselves is associated with a reduced risk of sleep deprivation in children.

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