Perceptions of unfairness and health complaints 50 years after Minamata disease outbreak

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Abstract

Despite increasing concern about the potential health effects of exposure to toxicological disasters, there is little consistent evidence regarding the role of psychosocial factors in exposure-symptom associations.

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We used data from a 2006 sampling survey of residents of the Shiranui Sea region of Japan to investigate whether perceptions of unfairness affected the association between methylmercury exposure and health complaints. A significant association was found between estimated methylmercury exposure and the prevalence of health complaints. When data were adjusted for perceptions of unfairness, the exposure-symptom association was substantially reduced, but a significant dose-response relationship remained. The present results suggest that exposure and perceptions of unfairness are important joint determinants of subsequent health complaints in Shiranui Sea communities. Community health care systems are needed to mitigate the increasing prevalence of perceived unfairness and to ease health complaints.

Key words: health complaints; methylmercury; perception of unfairness; psychosocial factor; toxicological disaster

Introduction

Despite increasing concerns about the potential health effects of exposure to toxicological disasters, there is little consistent evidence regarding the role of psychosocial factors in exposure-symptom associations. Minamata disease (MD) is a neurological disorder caused by consumption of methylmercury-contaminated seafood. Although more than 50 years have passed since the first outbreaks of MD in Japan, reports of ill health related to MD increased sharply following a ruling by the Supreme Court of Japan in October 2004[1-3]. The ruling compelled the Japanese government to pay damages to MD patients. This suggests that even the effects of biological events on ill health can be shaped by social and psychological conditions. We investigated whether MD-related psychosocial factors plays a critical role in association between methylmercury exposure and ill health, using the data from a sampling survey of residents of coastal Shiranui Sea communities in 2006, referred to as the 'Shiranui Study'.

Many studies have reported that exposure to toxic substances in the environment causes psychological distress in addition to pathological changes[4]. As pointed out by Spurgeon[5], the reporting of symptoms represents the outcome of a complex set of interactions between aspects of personality, attitude, culture, and social climate in addition to any pathological changes. Symptoms and complaints are essentially transactional in nature in the sense that the various biological, psychological, and social factors serve to reinforce and amplify one another. Therefore, health complaints made by residents may have arisen not only from pathological changes attributed to methylmercury exposure, but also from psychosocial factors such as stressful events related to the MD outbreak[6,7]. The results of a previous paper by our group suggested that the long-term struggles of MD victims for compensation from the company responsible and from the national government have been associated with elevated physical symptoms and psychological distress[8]. Furthermore, from the survey conducted in 2006, perceived unfairness of the MD compensation system is associated with inequality in health between MD victims and subjects certified earlier as MD patients[3]. Perceived unfairness is likely to be potential psychosocial distress in coastal Shiranui Sea communities. Since the importance of perceived unfairness had been established, the purpose of this study was to test the hypothesis that perceived unfairness was not only a contributor to patterns of reporting symptoms, but also a central, irreducible determinant of those patterns in addition to methylmercury exposure.

A few studies have investigated health complaints in patients certified as suffering from MD, or residents of highly polluted fishing villages or nearby areas[9,10]. However, there is evidence that residents of coastal Shiranui Sea communities, including non-fishing, agricultural and mountain villages also ate contaminated fish received from fishmongers or from relatives who were fishermen[11]. However, no systematic epidemiological studies have been undertaken in the Shiranui Sea

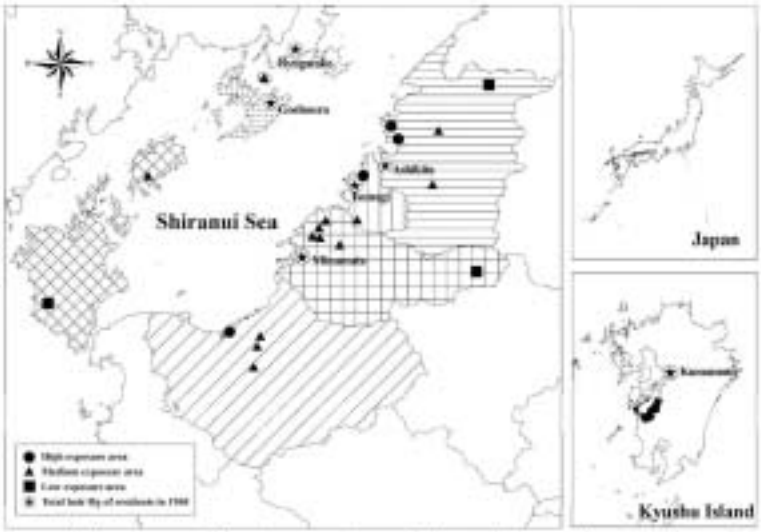
communities, despite more than 50 years having passed since the first outbreaks of MD. For the first time in the long history of the study of MD, we randomly sampled residents from all Shiranui Sea communities in September 2006 to investigate the relationship between methylmercury exposure and ill health.

Methods

Study population

We used data from a sampling survey of residents living in all the Shiranui Sea communities (Shiranui Study). The details have been described elsewhere[3]. Briefly, the study was conducted in 2006 and the subjects were residents aged 40-79 years residing in 172 postal code areas across six local government regions in the Shiranui Sea area (Figure 1). The total population aged 40-79 years in Shiranui Sea communities was almost 59,000. A postal code area corresponds approximately to an 'ooaza', which is the minimum size of a residential area in Japan. We defined the certified patients with MD and those who received payments and medical benefits in 1995 as early MD compensation recipients. The 172 postal code areas in the study included about 85% of all early MD compensation recipients.

The subjects were selected using a two-stage stratified protocol prespecified in a written random sampling plan, to ensure precision of the estimates in each stratum with different demographic characteristics and to yield a representative sample from each stratum. Before the first sampling, we determined strata by classifying the 172 postal code areas into eight strata according to the population per postal code area ($\leq$ 499, 500 to 999 and $\geq$ 1000), and the number of early MD compensation recipients (0, 1-9, 10-99 and $\geq$ 100). The population per postal code area was obtained from the 2000 Population Census of Japan[12], and the number of early MD compensation recipients in each postal code area was obtained from the local governments of Kumamoto and



Village		Minamata	Tsunagi	Ashikita	Goshoura	Ryugotake	Kumamoto
Median	ppm	50.0	33.0	48.6	21.5	17.5	2.1
Interquartile range	ppm	59.8	35.8	33.7	24.0	19.3	1.3

Figure 1. Study area

The shaded areas show the six local government regions in the Shiranui Sea area that were selected as the study area. This figure is taken from Ninomiya et al., 2005, which reported on hair samples that were collected from residents of the Shiranui Sea coastal area in 1960.

Kagoshima prefectures. In the first stage, we sampled 20 postal code areas randomly from the resulting eight strata with a probability proportional to the size of their populations. In the second stage, we sampled 105 residents (one person per household) per postal code area randomly. Questionnaires were mailed to the eligible subjects in August 2006 and these were collected 1-2 weeks later during a home visit. If the eligible subjects were absent during the visit or had not completed the questionnaire even after repeated visits, they were asked to return the completed questionnaire by mail using a stamped addressed envelope. The overall response proportion was 73.7% (1,548). Of these, 1,297 were collected by a home visit and 251 by mail. All subjects

gave informed consent to participate in the study, which was approved by the Ethics Committee of Fukuoka University.

Measurement of exposure

Methylmercury had been released from the Chisso Corporations Minamata factory into Minamata Bay for more than a decade. The first outbreaks of MD occurred in 1953-1956 around Minamata Bay on Kyushu, the southernmost of Japan's four main islands[13]. In 1958, the factory rebuilt its wastewater drainage channel to divert wastewater directly into the Minamata River[14]. This resulted in further dissemination of the pollution into the surrounding waters of the Shiranui Sea. Although the discharge of wastewater was stopped in 1968, the pollution affected fish up to the early 1970s[15]. Because fishing in that part of the Shiranui Sea was never restricted, people living in communities around the Shiranui Sea were exposed to methylmercury by ingestion at least until the early 1970s, which was confirmed by the presence of mercury in umbilical cords[16].

No data were available regarding the mercury levels in any of the residents in our study area. However, previous studies indicated that the median value of total mercury in hair samples of 1644 residents of the coastal fishing areas was 23.4 ppm (range, 0-920 ppm) in 1960 (Figure 1)[17]. The median values were 30.0 ppm in the Minamata area, 33.0 ppm in the Tsunagi area located 9 km away from Minamata, and 48.6 ppm in the Ashikita area located 14 km away from Minamata. On the other side of the Shiranui Sea, it was 21.5 ppm in the island of Goshoura and 17.5 ppm in the Ryugatake area. Although we have no information on all the inland Shiranui Sea communities, an investigation of family dietary habits in a methylmercury-polluted coastal fishing village indicated that fish and shellfish consumption was 2- to 4-fold higher than that of families living inland by near a fishing village[18]. We assumed that the geographical distance of the study area from the Shiranui Sea would be associated with the ingested amount of

contaminated seafood. Therefore, we categorized the 20 postal code areas into three areas according to their location or distance from the Shiranui Sea. The high exposure area was the coastal fishing areas facing the Shiranui Sea, the medium exposure area was the coastal fishing areas located on the other side of the Shiranui Sea or located within 5 km of the Shiranui Sea, and the low exposure area was located more than 5 km away from the sea or faced the East China Sea. The proportions of early MD compensation recipients per postal code area categorized in high, medium and low exposure areas were 26-67%, 1-10% and 0%, respectively.

Measurement of health complaints

Although patients with MD typically exhibit neurological signs such as ataxia, speech impairment, constriction of the visual field, and sensory disturbances[19,20], MD-related health problems are not necessarily limited to neurological disorders. In accord with this notion, a large proportion of uncertified patients show not only the typical neurological disorders of MD but also a varied, yet strikingly similar array of symptoms and complaints[2,10,21].

Health complaints were assessed by determining five characteristic complaints of MD: numbness in extremities, loss of sensation in extremities, difficulty in buttoning clothes, cramps in extremities and stumbling[10]. We also recorded five complaints reported by the general population to examine the prevalence of nonspecific, subclinical complaints according to putative methylmercury exposure: fatigue, headache, lower back pain, shoulder stiffness and arthralgia[22]. On the questionnaire, each subject was asked to report the frequency of experiencing a specified set of subjective complaints over the prior 30 days. Each health complaint response was scaled from no symptom, rarely, sometimes and always. The frequency of each complaint was categorized dichotomously (0 = no symptom or rarely; 1 = sometimes or always) for the analysis.

Measurement of perception of unfairness

The majority of inhabitants of the Shiranui Sea communities were exposed to various extents of methylmercury pollution, so that approximately 200,000 people are estimated to have been exposed[1]. From 1956 to 2008, the Kumamoto and Kagoshima prefectural government committees certified more than 2,200 residents as eligible for compensation as patients with MD. Because the government's definition of MD is too narrow, many uncertified patients have been excluded. In 1995 political settlement, approximately 11,000 residents received lump-sum payments and medical benefits-not for patients with MD but as victims heavily affected by methylmercury exposure. Furthermore, reports of ill health related to MD increased sharply after the 2004 Supreme Court's decision. In addition to about 6,600 uncertified patients applying for official recognition as MD patients, about 27,000 uncertified patients are currently receiving medical subsidies in return for having withdrawn their applications for certification.

The populations that received some MD compensation were a socially excluded minority within their community, as the communities had oppressive attitudes to the uncertified patients at that time seeking compensation. Thus, receiving a certain kind of MD compensation had been a major source of stigma and discrimination in the community, at least until the 1995 political settlement. However, neighborhood social circumstances with regard to MD compensation changed markedly following the 1995 political settlement, and receiving MD compensation is no longer regarded as a stigma because the sizes of populations receiving compensation have greatly increased. Some people who did not receive MD compensation, and particularly those with poor health, perceived unfairness in the 1995 political settlement.

Perceived unfairness of 1995 political settlement was measured by the following single-item question: "Would you say the political settlement in 1995 was fair or unfair?". The perceived unfairness of the settlement was classified into two categories: 0=fair, almost fair; and

1=slightly unfair, unfair.

Demographic characteristics

Information on demographic and social characteristics was obtained from the self-administered questionnaire. Age was classified into four categories: 40-49, 50-59, 60-69 and 70-79 years. Education attainment was classified into three categories: ≤ 9, 10-12 and ≥ 13 years. Self-rated economic status was classified into four categories: more than satisfactory, satisfactory, insufficient, and very insufficient. The frequency of consuming methylmercury contaminated seafood in 1950-1968 was classified into five categories: ≤ once weekly, 2-3 times weekly, 4-6 times weekly, once daily and ≥ twice daily.

Data retrieval for analysis

To identify appropriate data for our analysis, we first excluded those data missing information on gender, age and area (n = 1,482). Our analysis was then further limited to the 750 participants who had lived in their current residence for more than 40 years.

Statistical analysis

We used the χ^2, Mantel-Haenszel test and one-way analysis of variance (ANOVA) to calculate P value for the differences of distribution of demographic and psychosocial factors by exposure area. Age-specific prevalence of each subjective complaint was calculated by exposure area. The differences in prevalence were compared among exposure area by age using the Mantel-Haenszel test.

We estimated the adjusted prevalence odds ratios of the subjective complaints in relation to exposure using a logistic regression model. From this analysis, we calculated odds ratios (OR) with 95% confidence intervals (CI). The baseline model was adjusted for gender, age, education and self-rated economic status. Subsequent models were also adjusted for perception of unfairness to investigate whether perception of

unfairness was a potential confounder examining the relationship between methylmercury exposure and health complaints. We performed the descriptive and logistic regression analysis using SAS software (Release 9.1; SAS Institute Inc., Cary, NC, USA).

Results

The overall response proportions in the Shiranui Study were 73.7%. In the first stage excluding missing data, the response proportions were 76.4%, 70.0% and 65.1%, in high, medium and low exposure areas, respectively. In the second stage excluding those subjects not meeting the target history of residence, the response proportions were 46.9% (n = 197), 31.0% (n = 423) and 41.3% (n = 130), respectively.

The demographic characteristics of the subjects are shown in Table 1. Those who lived in the high or low exposure areas tended to have less education, and those who lived in the high exposure area believed that they had a lower economic status. There was a greater reported intake of seafood in the high versus the low exposure areas. There was a tendency for an increase in the reporting of the higher levels of unfairness of the 1995 political settlement by subjects from low- to high-exposure areas. Forty-two percent of the subjects in high exposure area perceived unfairness. There were no significant differences in gender or age among the residents living in each exposure area. The prevalence of subjective complaints, except for fatigue, headache, lower back pain and shoulder stiffness tended to increase in subjects more than 60 years of age, regardless of exposure area (Table 2). Among the residents aged 70-79 years old in high exposure area, the prevalence of all subjective complaints was significantly higher than other exposure area.

Subjects in the high exposure area had the highest prevalence of all complaints (Table 3). The medium exposure area had an intermediate prevalence of all complaints, except for arthralgia. The prevalence of fatigue, lower back pain and shoulder stiffness in the subjects from the

Table 1. Demographic Characteristics of Subjects, by Study Area

	Low	Medium	High	*p*
Gender				
Male	69 (53.1)*	223 (52.7)	97 (49.2)	0.689
Female	61 (46.9)	200 (47.3)	100 (50.8)	
Age (yr)				
40-49	8 (6.2)	25 (5.9)	17 (8.6)	0.621
50-59	21 (16.2)	83 (19.6)	33 (16.8)	
60-69	37 (28.5)	136 (32.2)	57 (28.9)	
70-	64 (49.2)	179 (42.3)	90 (45.7)	
Education(yr)				
≤9	72 (55.4)	161 (38.1)	99 (50.3)	0.0005
10-12	53 (40.8)	190 (44.9)	74 (37.6)	
≥13	5 (3.9)	59 (14.0)	19 (9.6)	
Unknown	0 (0.0)	13 (3.1)	5 (2.5)	
Self-rated economic status				
More than satisfactory	3 (2.3)	8 (1.9)	0 (0.0)	0.050
Satisfactory	37 (28.5)	134 (31.7)	41 (20.8)	
Insufficient	63 (48.5)	187 (44.2)	111 (56.4)	
Very insufficient	25 (19.2)	87 (20.6)	44 (22.3)	
Unknown	2 (1.5)	7 (1.7)	1 (0.5)	
Frequency of eating seafood				
≤once/week	51 (39.2)	65 (15.4)	6 (3.1)	<.0001
2～3 times/week	42 (32.3)	115 (27.2)	19 (9.6)	
4～6 times/week	14 (10.8)	77 (18.2)	16 (8.1)	
Once/day	13 (10.0)	89 (21.0)	49 (24.9)	
≥2 times/day	7 (5.4)	69 (16.3)	106 (53.9)	
Unknown	3 (2.3)	8 (1.9)	1 (0.5)	
Perceived unfairness of the 1995 political settlement				
Fair/almost fair	106 (81.5)	311 (73.5)	111 (56.4)	<.0001
Slightly unfair/unfair	17 (13.1)	97 (22.9)	82 (41.6)	
Unknown	7 (5.4)	15 (3.6)	4 (2.0)	

* number (%)

low exposure area were 53.5%, 70.9%, and 64.8%, respectively, whereas in the high exposure area the corresponding proportions were 81.1%, 84.8% and 81.2%, respectively.

The results of the logistic model, after adjusting for gender, age, education and self-rated economic status, were shown in Table 3. A significant association was observed between the level of exposure and the prevalence of all complaints. The OR values for the prevalence of

Table 2. Prevalence Proportions of Subjective Complaints, by Age and Exposure Area

		40-49	*p*	50-59	*p*	60-69	*p*	70-79	*p*
Numbness in the extremities	Low	3 (37.5)*	0.505	6 (28.6)	0.075	15 (41.7)	<.0001	26 (41.3)	<.0001
	Medium	8 (32.0)		38 (46.9)		74 (54.8)		103 (59.5)	
	High	8 (47.1)		18 (54.6)		47 (82.5)		80 (88.9)	
Loss of sensation in the extremities	Low	1 (12.5)	0.032	4 (20.0)	0.006	14 (38.9)	<.001	19 (30.7)	<.0001
	Medium	7 (28.0)		25 (30.9)		62 (46.3)		79 (45.7)	
	High	9 (52.9)		18 (54.6)		43 (75.4)		77 (86.5)	
Difficulty in buttoning	Low	2 (25.0)	0.402	5 (25.0)	0.131	12 (33.3)	<.001	19 (31.2)	<.0001
	Medium	8 (32.0)		22 (27.2)		58 (43.0)		80 (46.0)	
	High	7 (41.2)		14 (42.4)		39 (68.4)		68 (75.6)	
Cramps in the extremities	Low	2 (25.0)	0.131	8 (40.0)	0.540	18 (58.1)	0.067	31 (50.0)	<.0001
	Medium	8 (32.0)		34 (44.2)		73 (55.3)		86 (51.5)	
	High	9 (52.9)		16 (48.5)		42 (73.7)		72 (80.0)	
Stumbling	Low	0 (0.0)	0.030	6 (30.0)	0.261	18 (50.0)	0.031	31 (49.2)	<.0001
	Medium	6 (24.0)		23 (28.8)		70 (51.9)		104 (59.4)	
	High	7 (41.2)		14 (42.4)		40 (70.2)		75 (83.3)	
Fatigue	Low	4 (50.0)	0.089	12 (57.1)	0.048	19 (52.8)	0.005	34 (53.1)	<.001
	Medium	16 (64.0)		55 (67.9)		92 (68.2)		115 (65.7)	
	High	14 (82.4)		27 (81.8)		46 (80.7)		72 (80.9)	
Headache	Low	1 (12.5)	0.132	5 (23.8)	0.195	13 (38.2)	0.089	21 (33.3)	<.0001
	Medium	14 (56.0)		23 (28.4)		67 (50.0)		71 (40.8)	
	High	9 (52.9)		13 (39.4)		32 (57.1)		58 (65.2)	
Lower back pain	Low	5 (62.5)	0.206	12 (60.0)	0.186	27 (75.0)	0.478	46 (73.0)	0.003
	Medium	15 (60.0)		50 (61.7)		103 (75.7)		137 (79.2)	
	High	14 (82.4)		25 (75.8)		46 (80.7)		82 (91.1)	
Shoulder stiffness	Low	4 (50.0)	0.505	10 (52.6)	0.124	25 (69.4)	0.056	42 (67.7)	0.003
	Medium	19 (76.0)		49 (59.8)		106 (77.9)		133 (75.6)	
	High	8 (47.1)		24 (72.3)		49 (86.0)		79 (87.8)	
Arthralgia	Low	3 (37.5)	0.182	11 (55.0)	0.728	23 (65.7)	0.201	45 (71.4)	0.033
	Medium	8 (32.0)		39 (48.8)		93 (68.4)		124 (70.9)	
	High	10 (58.8)		19 (57.6)		44 (77.2)		75 (85.2)	

* number (%)

Table 3. Association of Study Area with Subjective Complaints

		Prevalence	Adjusted oddsRatio*	*P* for trend	Adjusted odds Ratio†	*P* for trend
Numbness in the extremities	Low	50 (39.1)	1.00	<0.0001	1.00	<0.0001
	Medium	223 (53.9)	2.48 (1.60- 3.86)		2.53 (1.60- 4.01)	
	High	153 (77.7)	6.78 (3.98-11.55)		6.12 (3.52-10.65)	
Loss of sensation in the extremities	Low	38 (30.2)	1.00	<0.0001	1.00	<0.0001
	Medium	173 (41.9)	2.12 (1.34- 3.35)		2.12 (1.32- 3.42)	
	High	147 (75.0)	8.49 (4.96-14.53)		7.48 (4.27-13.10)	
Difficulty in buttoning	Low	38 (30.4)	1.00	<0.0001	1.00	<0.0001
	Medium	168 (40.5)	1.90 (1.21- 3.00)		1.73 (1.08- 2.76)	
	High	128 (65.0)	4.71 (2.83- 7.84)		3.79 (2.23- 6.42)	
Cramps in the extremities	Low	59 (48.8)	1.00	<0.0001	1.00	0.0006
	Medium	201 (50.1)	1.22 (0.80- 1.88)		1.16 (0.74- 1.80)	
	High	139 (70.6)	2.65 (1.62- 4.35)		2.30 (1.38- 3.84)	
Stumbling	Low	55 (43.3)	1.00	<0.0001	1.00	<0.0001
	Medium	203 (48.9)	1.50 (0.98- 2.32)		1.46 (0.93- 2.28)	
	High	136 (69.0)	3.38 (2.04- 5.60)		2.93 (1.73- 4.95)	
Fatigue	Low	69 (53.5)	1.00	<0.0001	1.00	<0.0001
	Medium	278 (66.8)	1.85 (1.22- 2.80)		1.66 (1.08- 2.55)	
	High	159 (81.1)	3.52 (2.12- 5.85)		2.85 (1.68- 4.82)	
Headache	Low	40 (31.8)	1.00	<0.0001	1.00	0.012
	Medium	175 (42.3)	1.81 (1.15- 2.84)		1.55 (0.98- 2.47)	
	High	112 (57.4)	2.84 (1.73- 4.68)		2.32 (1.39- 3.90)	
Lower back pain	Low	90 (70.9)	1.00	0.004	1.00	0.021
	Medium	305 (73.5)	1.34 (0.84- 2.15)		1.35 (0.84- 2.19)	
	High	167 (84.8)	2.29 (1.29- 4.06)		2.00 (1.11- 3.62)	
Shoulder stiffness	Low	81 (64.8)	1.00	0.002	1.00	0.029
	Medium	307 (73.3)	1.70 (1.09- 2.66)		1.53 (0.96- 2.43)	
	High	160 (81.2)	2.40 (1.41- 4.10)		1.88 (1.08- 3.29)	
Arthralgia	Low	82 (65.1)	1.00	0.014	1.00	0.051
	Medium	264 (63.5)	1.14 (0.73- 1.78)		1.07 (0.67- 1.71)	
	High	148 (75.9)	1.86 (1.10- 3.15)		1.68 (0.96- 2.92)	

* Adjustment for gender, age, education and self-rated economic status.
† Adjustment for gender, age, education, self-rated economic status and the perception of unfairness.

numbness in extremities, loss of sensation in extremities, difficulty in buttoning, fatigue, headache, shoulder stiffness in the subjects from the medium exposure area were significantly higher than in those from the low exposure area. Further adjustment for the perception of unfairness substantially reduced the relationship. However, a dose-

response relationship was still observed in all complaints except arthralgia. The OR values for the prevalence of numbness in extremities and loss of sensation in extremities in the subjects from the high exposure area were 6.12 and 7.48, respectively, compared with subjects in the low exposure area. Subjects in the medium exposure area had a significantly higher prevalence of numbness in extremities, loss of sensation in the extremities, difficulty in buttoning and fatigue compared with subjects in the low exposure area.

Discussion

In an analysis of data from the first random sampling and systematic epidemiological study of residents from all communities in the coastal Shiranui Sea region, we found evidence of a significant association between estimated methylmercury exposure and health complaints. Importantly, the results suggested that the exposure-symptom association was substantially reduced after adjusting for the perception of unfairness. These findings indicate that the association between exposure and health complaints is modified by the perception of unfairness. Therefore, exposure and perception of unfairness can be considered potentially important joint determinants of health complaints.

The highest proportion of respondents reporting the perception of unfairness was observed in high exposure areas, followed by medium exposure areas. People in high exposure areas were more likely to perceive unfairness if a high proportion of their family, friends or neighbors had been certified as MD patients or applied for MD compensation. This finding suggests that the perception of unfairness may be influenced by comparisons with members of the family or community. If the perception of unfairness was nothing other than an alternative measure of exposure level, this conclusion might be invalid. However, our earlier study indicated that although perceptions of unfairness and exposure level are correlated, they remain separable[3].

Thus, our results indicate that the perception of unfairness can account for a substantial proportion of the observed disparities in health reported by earlier studies.

Our other major finding was that a significant association between exposure and typical MD complaints along with general complaints remained even after adjusting for perception of unfairness. This finding suggests the possibility that the long-term effects of methylmercury exposure continue to affect people in exposed regions, despite a period of more than 50 years since the first outbreak. It is well known that the primary target organ of methylmercury poisoning is the central nervous system[23], and somatosensory disturbance appears to be the most important symptom of chronic or delayed methylmercury exposure[1, 2, 13]. The results of the present study suggest that reports of symptoms related to neurological disorders in residents of the high exposure area are significantly more common than in less exposed regions over a 60-year period. In addition, non-neurological symptoms and complaints in residents of high exposure area were significantly more common than in other areas over a 70-year period. Some previous studies have presented a model in which neuronal loss below a certain level results in no identifiable impairment, but can result in the development of neurological symptoms when combined with age-related neurological attrition[24-26]. Furthermore, a few studies have suggested that methylmercury exposure early in life can emerge later in the form of post-exposure syndromes[25, 26]. These post-exposure syndromes attributed to early methylmercury exposure might be associated with the typical neurological symptoms of MD but also a variety of non-neurological symptoms and complaints later in life.

However, there are several issues that must be taken into account when interpreting our findings. First, the participation rate of the survey was not perfect (76.4%, 70.0% and 65.1%, in high, medium and low exposure areas, respectively). It remains possible that residents who were not interested in MD-related health concerns were over-

represented in the group of people that did not participate in this study. If this were the case, it would be expected that people in low-exposure area would be less likely to participate in the survey. However, the response proportions in the present study were not significantly different between high and low exposure areas (46.9% and 41.3%, respectively), and the age or gender distributions of participants across each exposure area were not significantly different. Therefore, even if a self-selection bias existed in the present data set, such a bias could not have induced significant effects of the magnitude observed here.

Second, like the majority of studies concerned with the health effects of toxic chemical exposure, our study suffered from a lack of any accurate measurement of direct exposure. We based our assessment of methylmercury exposure primarily on surrogate measures such as the geographical location or distance of residential areas from the Shiranui Sea. These proxy variables are clearly crude markers of true exposure levels, and their validity is limited. When there are three or more exposure categories, non-differential exposure can result in either over- or underestimation of the effect in question[27]. However, all subjects in the present study had resided in the area for over 40 years, and the categorized areas corresponded with the self-reported frequency of consuming contaminated seafood. Therefore, even if there was a misclassification of the actual exposure, such a bias could not have induced the large effects observed here.

Third, our reference areas were located more than 5 km from the Shiranui Sea or faced the East China Sea and these areas had no early MD compensation recipients, distinguishing them clearly from the other exposure areas. However, contaminated fish or shellfish could have been carried by fishmongers or relatives to these areas, meaning that they may not have been entirely unexposed to methylmercury. As such, subjects categorized as living in low exposure area may not have been a purely unexposed population. The Comprehensive Survey of

Living Conditions of the People on Health and Welfare in Japan, which was conducted in the general population over 70 years of age, reported the prevalence of numbness in extremities, fatigue, headache, lower back pain, shoulder stiffness and arthralgia as 9.6%, 6.1%, 4.6%, 21.9%, 13.3% and 17.2%, respectively[21]. Although we cannot compare these findings with ours directly, the corresponding proportions in the low exposure area for subjects 70-79 years old were 41.3%, 53.1%, 33.3%, 73.0%, 67.7% and 71.4%, respectively. As shown by the present results, a high prevalence of general complaints such as fatigue or lethargy, headache, lower back pain, shoulder stiffness and arthralgia was frequently reported in patients with chronic MD, and particularly among the residents of highly contaminated areas[2, 10]. These results suggest that, if anything, using low exposure area as a reference might lead to an underestimation of the exposure effect.

The fourth limitation is related to the cross-sectional design of this study, which limits the degree to which causality can be assigned. In addition, this study was unable to include subjects who left the communities because of poor health or fishery industry depression, who were institutionalized elsewhere, or who died from methylmercury poisoning. It seems a reasonable assumption that such individuals are more likely to have resided in high exposure area, given the reported proportions of early MD compensation recipients. Therefore, any selection bias from omitting these 'missing' subjects would be expected to have caused an underestimation of the true magnitude of the effects.

Despite these limitations, our findings are noteworthy for four major reasons. First, this study is the first random sampling examination of residents from all of the communities in the coastal Shiranui Sea region to be undertaken with rigorous standards of systematic data collection. Second, this study suggests that exposure and perception of unfairness are potentially important joint determinants of health complaints throughout communities in the coastal Shiranui Sea region. Third, the results clearly indicate that even residents in the

medium exposure area suffered from not just the typical MD-related neurological disorders but also a variety of non-neurological symptoms and complaints. Forth, our findings show that the subjects exposed to methylmercury earlier in life may exhibit an increased prevalence of post-exposure syndromes such as typical MD complaints, as well as general complaints later in life. Understanding the role of the perception of unfairness in the etiology of physical symptoms is important for prevention of this characteristic disease burden in the community. Our findings indicate that community health care systems should be boosted to ease typical MD and non-specific symptoms and to mitigate the increasing prevalence of perception of unfairness.

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