Dr. Masaaki Nakamura

○アブストラクトデータ

Methylmercury exposure and neurological outcomes in Taiji, the birthplace of traditional whaling in Japan

Masaaki Nakamura, Ken-ya Murata, Ichiro Nakanishi, Akira Yasutake, Noriyuki Hachiya, Ken-ichiro Miyamoto, Mineshi Sakamoto, Fusako Usuki, Tomoyoshi Kondo

Methylmercury (MeHg) exposure occurs primarily through the consumption of fish, but the environmental threat to human health is poorly understood. Taiji is famous as the birthplace of traditional whaling in Japan, and the geometric mean hair mercury level is reportedly higher than that in the general Japanese population. However, the investigation of the health impact associated with MeHg in Taiji residents has not been performed so far. Our study aimed to determine whether there were undesirable health consequences (especially neurological abnormalities) with MeHg exposure in Taiji. After a preceding hair mercury survey (724 residents) to assess MeHg exposure, the subjects of the present study (194 residents) underwent a neurological examination. Audiometry, MRI, and EMG were performed for the subjects with hearing impairment or sensory disturbance. The geometric mean of hair mercury of the male and female subjects was 9.97 and 6.19 ppm in the preceding hair mercury survey and 17.2 and 12.1 ppm in the present study. Hair mercury levels of 2.2% subjects (preceding hair mercury survey) and 6.2% subjects (present study) were higher than 50 ppm, the level for NOAEL set by WHO. No subject presented with the perioral sensory disturbance which was often present in MeHg poisoning. Taken together with the neurological findings and laboratory results of MRI and EMG, sensory disturbance was diagnosed as follows: cervical spondylosis (3 subjects), cervical spinal canal stenosis (3 subjects), lumbar spondylosis (2 subjects), lumbar spinal canal stenosis (3 subjects), lumbar disk herniation (one subject), carpal tunnel syndrome (3 subjects), ulnar palsy (one subject), polyneuropathy (5 subjects), carpal tunnel syndrome (3 subjects), ulnar palsy (one subject), sciatic pain (one subject), and tarsal tunnel syndrome (one subject). Two among 12 subjects beyond 50 ppm showed a decrease of vibratory sensation, but ataxia and abnormality of combined sensation (two-point discrimination, graphesthesia, and stereognostic sense), which was often present in MeHg poisoning, were not seen. There was no dose-response relationship between hair mercury levels and all neurological signs, although a dose-response relationship was observed between age and some neurological signs. These findings suggested that the apparent adverse effects of MeHg exposure on neurological symptoms may not follow MeHg exposure in Taiji. A future study is warranted to determine the reason why clear undesirable health consequences were not seen despite the high MeHg exposure.

○発表データ

NIMD

Methylmercury exposure and neurological outcomes in Taiji, the birthplace of traditional whaling in Japan

National Institute for Minamata Disease

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Background

1. WHO has announced in 1990 that a hair mercury level of 50–125 ppm corresponds to "no observed adversary effect level" (NOAEL) of MeHg for adults.

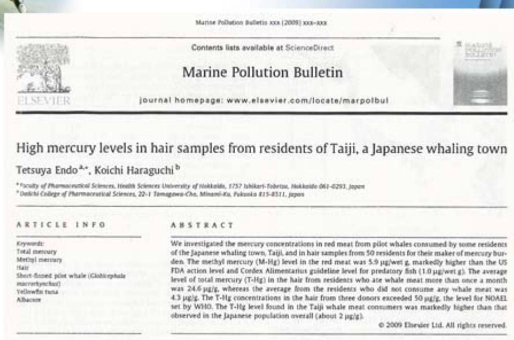
2. Afterwards, however, there have been some reports (Amazonian studies) suggesting the possible MeHg intoxication in adults whose hair mercury levels are below 50 ppm.

The threshold level that MeHg toxicity elicits in adults is still controversial.

Taiji

- The birthplace of traditional whaling in Japan
- The majority of the townsman engaged in whaling and whaling -related work in the past.

Taiji



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High mercury levels in hair samples from residents of Taiji, a Japanese whaling town

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ABSTRACT

We investigated the mercury concentrations in red meat from pilot whales consumed by some residents of the Japanese whaling town, Taiji, and in hair samples from 50 residents for their maker of mercury burden. The methyl mercury (M-Hg) level in the red meat was 5.9 μg/wet g, markedly higher than the US FDA action level and Codex Alimentarius guideline level for predatory fish (1.0 μg/wet g). The average level of total mercury (T-Hg) in the hair from residents who ate whale meat more than once a month was 24.6 μg/g, whereas the average from the residents who did not consume any whale meat was 4.3 μg/g. The T-Hg concentrations in the hair from three donors exceeded 50 μg/g, the level for NOAEL set by WHO. The T-Hg level found in the Taiji whale meat consumers was markedly higher than that observed in the Japanese population overall (about 2 μg/g).

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Purpose

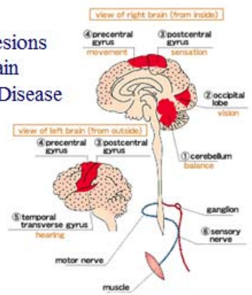
The aim of this study is to investigate health effects of MeHg on adults.

Methods- 1

1) preceding hair mercury survey: 724 residents (344 males and 380 females)

Methods- 1

Localized lesions of the brain in Minamata Disease



Methods- 1

1) preceding hair mercury survey: 724 residents (344 males and 380 females)

2) Detailed neurological examination

a) Objects:194 residents (117 males and 77 females)

b) Neurological examination: three certified neurologists, authorized by the Japanese Society of Neurology

c) Detailed examination: audiometry: 32 subjects
MRI: brain: 8 subjects;
cervical: 10 subjects;
lumbar: 9 subjects)
EMG: 24 subjects

Methods- 2

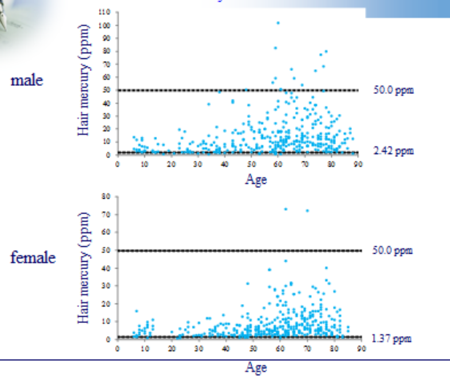
3) Analysis of health consequence by MeHg

a) Clinical evaluation

b) Associations between the neurological outcomes and hair mercury concentration, age and gender.

c) Detailed assessment of 12 residents whose mercury concentrations were over 50 ppm, the level for NOAEL set by WHO

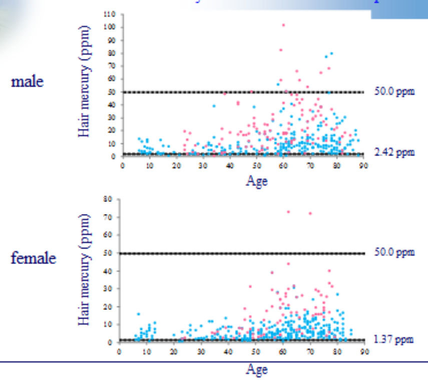
Distribution of hair mercury concentration of the 724 residents



Distribution of hair mercury concentration of the 724 residents

Gender	male	female	total
N	344	380	724
Age (years)			
Min	6	6	6
Max	88	92	92
Arithmetic mean	57.5	56.4	56.9
Hair mercury (μg/g)			
Min	0.6	0.7	0.6
25 Percentile	5.1	3.5	4.0
Median	10.6	5.9	7.7
75 Percentile	19.5	11.0	14.6
Max	101.9	73.1	101.9
Geometric mean	10.0	6.2	7.8
Hair mercury ≧ 50 μg/g (N)	14	2	16

Distribution of hair mercury concentration of the present study



Distribution of hair mercury concentration of the present study

Gender	male	female	total
N	117	77	194
Age (years)			
Min	20	24	20
Max	85	79	85
Arithmetic mean	56.7	59.5	57.8
Hair mercury (μg/g)			
Min	1.1	2.1	1.1
25 Percentile	11.1	5.9	7.9
Median	18.7	15.1	17.8
75 Percentile	32.7	24.3	28.7
Max	101.9	73.1	101.9
Geometric mean	17.2	12.1	14.9
Hair mercury ≧ 50 μg/g (N)	10	2	12

Summary of Neurologic diagnosis

clinical diagnosis	N
polyneuropathy	13
multiple cerebral infarction	2
late effects of cerebral infarction	1
parkinsonism	1
postural tremor	4
cervical spondylosis	5
cervical spinal canal stenosis	4
cervical disc herniation	1
thoracic outlet syndrome	1
carpal tunnel syndrome	4
ulnar palsy	1
birth palsy	1
lumbar spinal canal stenosis	3
lumbar spondylosis	2
lumbar disk herniation	2
sciatic pain	1
tarsal tunnel syndrome	1
Minamata disease (MeHg poisoning)	0

Associations of neurologic findings with hair mercury concentrations, age and gender-1

Neurologic findings		analysis	Adjusted odds ratios or adjusted regression coefficients (95% confidence interval if calculated)		
			age	male (female as a referent)	hair mercury concentration log (ppm)
cranial nerve	sensorineural hearing loss	logistic regression	1.05 (1.00, 1.10	1.56 (0.44, 5.49)	1.22 (0.22, 6.89)
muscular weakness	upper limb	logistic regression	0.94 (0.86, 1.03	0.13 (0.010, 1.65)	3.37 (0.13, 85.7)
	lower limb	logistic regression	1.02 (0.91, 1.14	0.12 (.010, 1.31)	47.7 (0.77, 2950)
tremor	postural	logistic regression	1.12 (1.04, 1.21 **	1.10 (0.29, 4.21)	2.63 (0.031, 22.2)
coordinated movement	diadocho - kinesis	logistic regression	1.25 (1.03, 1.51 *	1.32 (0.12, 15.0)	16.8 (0.22, 1280)
	finger-to-nose test	logistic regression	1.19 (0.98, 1.44	2.25x10^7 (-)	3.22 (0.03 413)
	heel-knee test	logistic regression	1.12 (1.03, 1.21 **	5.14 (0.57, 46.2)	0.67 (0.07, 6.81)
	knee tapping test	logistic regression	1.11 (1.00, 1.24	4.88x10^7 (-)	4.87 (0.14, 172)
one foot standing	right foot ≥ 5s	logistic regression	1.12 (1.02, 1.23 *	1.38 (0.23, 8.15)	1.97 (0.14, 27.3)
	right foot ≥ 15s	logistic regression	1.11 (1.06, 1.16 ***	0.70 (0.30, 1.67)	2.05 (0.58, 7.25)
	left foot ≥ 5s	logistic regression	1.11 (1.02, 1.21 *	0.64 (0.15, 2.76)	2.55 (0.25, 25.9)
	left foot ≥ 15s	logistic regression	1.12 (1.07, 1.17 ***	0.83 (0.35, 1.97)	1.87 (0.53, 6.59)
simple gait		logistic regression	1.11 (0.98, 1.25	1.65 (0.16, 16.7)	31.1 (0.56, 1760)
tandem gait		logistic regression	1.22 (1.03, 1.45 *	3.23x10^7 (-)	5.60 (0.08, 392)

reflex	upper limb	logistic regression	1.05 (1.02, 1.08) **	2.86 (1.25, 6.46) *	1.04 (0.36, 2.99)
	lower limb	logistic regression	1.05 (1.02, 1.09) **	1.67 (0.77, 3.65)	1.22 (0.42, 3.57)
	Babinski	logistic regression	1.15 (0.98, 1.35)	0.38 (0.04, 3.36)	11.2 (0.18, 681)
	Chaddock	logistic regression	1.15 (0.98, 1.35)	0.38 (0.04, 3.36)	11.2 '0.18, 681)
touch sensation		logistic regression	1.07 (1.03, 1.12) **	1.58 (0.53, 4.65)	0.55 (0.13, 2.39)
pain sensation		logistic regression	1.06 (1.02, 1.10) **	1.03 (0.40, 2.68)	0.79 (0.21, 3.02)
vibratory sense	right upper limb (s)	linear regression	-0.087 (-0.12, -0.055) ***	0.21 (-0.69, 1.11)	-0.68 (-1.90, 0.55)
	left upper limb (s)	linear regression	-0.081 (-0.11, -0.052) ***	-0.018 (-0.82, 0.80)	-0.38 (-1.49, 0.74)
	right lower limb (s)	linear regression	-0.15 (-0.18, -0.12) ***	0.24 (-0.57, 1.05)	-0.35 (-1.46, 0.75)
	left lower limb (s)	linear regression	-0.15 (-0.18, -0.12) ***	-0.062 (-0.84, 0.71)	0.12 (-0.94, 1.18)
two-point discrimination	right index finger (mm)	linear regression	0.017 (-0.002, 0.036)	-0.37 (-0.89, 0.15)	0.31 (-0.41, 1.02)
	left index finger (mm)	linear regression	0.022 (0.000, 0.043)	-0.34 (-0.95, 0.26)	0.26 (-0.57, 1.09)
graphesthesia	right palm (/4)	linear regression	-0.001 (-0.002, 0.001)	-0.004 (-0.042, 0.033)	-0.009 (-0.060, 0.042)
	left palm (/4)	linear regression	-0.001 (-0.002, 0.001)	0.039 (-0.021, 0.10)	-0.049 (-0.13, 0.032)
stereognosis (/3)		linear regression	0.000 (-0.001, 0.001)	-0.018 (-0.048, 0.012)	-0.002 (-0.064, 0.060)

Associations of neurologic findings with hair mercury concentrations, age and gender-2

	Range of hair mercury concentration of four quartiles
1	1.1 ppm to 7.9 ppm
2	7.9 ppm to 17.8 ppm
3	17.8 ppm to 28.7 ppm
4	28.7 ppm to 101.9 ppm

Associations of neurologic findings with hair mercury concentrations, age and gender-2

Neurologic findings		analysis	Adjusted odds ratios or adjusted regression coefficients (95% confidence interval if calculated)		
			age	male (female as a referent)	hair mercury concentration Quartile 4 (Quartile 1 as a referent)
cranial nerve	sensorineural hearing loss	logistic regression	1.05 (0.98, 1.12)	5.80 (0.57, 59.2)	0.45 (0.07, 2.95)
muscular weakness	upper limb	logistic regression	0.91 (0.77, 1.08)	$2.96x10^{6}$ (-)	$5.22x10^{7}$ (-)
	lower limb	logistic regression	1.02 (0.87, 1.19)	0.28 (0.02, 4.83)	$8.91x10^{7}$ (-)
tremor	postural	logistic regression	1.15 (0.96, 1.38)	0.17 (0.02, 1.76)	$1.37x10^{6}$ (-)
coordinated movement	diadocho - kinesis	logistic regression	1.18 (0.89, 1.57)	$1.35x10^{7}$ (-)	$1.22x10^{7}$ (-)
	finger-to-nose test	logistic regression	1.03 (0.83, 1.28)	$9.38x10^{6}$ (-)	$9.11x10^{6}$ (-)
	heel-knee test	logistic regression	1.09 (0.98, 1.22)	$1.23x10^{6}$ (-)	0.58 (0.04, 7.58)
	knee tapping test	logistic regression	1.12 (0.92, 1.35)	$2.68x10^{7}$ (-)	$1.64x10^{7}$ (-)
one foot standing	right foot < 5s	logistic regression	1.42 (1.03, 1.98) *	$1.53x10^{6}$ (-)	0.50 (0.00, 82.0)
	right foot < 15s	logistic regression	1.21 (1.08, 1.35) **	1.15 (0.21, 6.34)	2.40 (0.35, 16.6)
	left foot < 5s	logistic regression	$1.03x10^{10}$ (-)	$7.62x10^{6}$ (-)	$8.12x10^{21}$ (-)
	left foot < 15s	logistic regression	1.21 (1.08, 1.35) **	1.15 (0.21, 6.34)	2.40 (0.35, 16.6)
simple gait		logistic regression	1.03 (0.91, 1.18)	$2.97x10^{7}$ (-)	$2.83x10^{7}$ (-)
tandem gait		logistic regression	1.22 (0.94, 1.58)	$1.97x10^{7}$ (-)	$2.23x10^{7}$ (-)

reflex	upper limb	logistic regression	1.03 (0.98, 1.08)	4.57 (0.89, 23.6)	1.45 (0.33, 6.31)
	lower limb	logistic regression	1.08 (1.02, 1.13) **	1.19 (0.36, 3.96)	0.94 (0.26, 3.36)
	Babinski	logistic regression	1.03 (0.83, 1.28)	$9.38x10^{6}$ (-)	$9.11x10^{6}$ (-)
	Chaddock	logistic regression	1.03 (0.83, 1.28)	$9.38x10^{6}$ (-)	$9.11x10^{6}$ (-)
touch sensation		logistic regression	1.04 (0.98, 1.11)	0.85 (0.15, 4.79)	0.92 (0.15, 5.78)
pain sensation		logistic regression	1.04 (0.97, 1.11)	0.51 (0.10, 2.54)	1.51(0.26, 8.79)
vibratory sense	right upper limb (s)	linear regression	-0.076 (-0.12, -0.029) **	-0.018 (-1.36, 1.33)	-0.95 (-2.46, 0.57)
	left upper limb (s)	linear regression	-0.081 (-0.12, -0.039) ***	-0.21 (-1.41, 1.00)	-0.40 (-1.75, 0.96)
	right lower limb (s)	linear regression	-0.15 (-0.19, -0.11) ***	0.62 (-0.59, 1.84)	-0.84 (-2.21, 0.53)
	left lower limb (s)	linear regression	-0.14 (-0.18, -0.10) ***	0.37 (-0.76, 1.49)	-0.38 (-1.65, 0.89)
two-point discrimination	right index finger (mm)	linear regression	0.008 (-0.017, 0.032)	-0.42 (-1.14, 0.29)	0.50 (-0.30, 1.31)
	left index finger (mm)	linear regression	0.017 (-0.015, 0.048)	-0.43 (-1.34, 0.48)	0.36 (-0.66, 1.38)
graphesthesia	right palm (/4)	linear regression	0.000 (-0.002, 0.001)	-0.012 (-0.058, 0.033)	-0.013 (-0.064, 0.038)
	left palm (/4)	linear regression	-0.001 (-0.004, 0.002)	0.010 (-0.067, 0.087)	-0.050 (-0.14, 0.037)
stereognosis (/3)		linear regression	NA [b]	NA [b]	NA [b]

Associations of neurologic findings with hair mercury concentrations, age and gender-3

Neurologic findings		analysis	Adjusted odds ratios or adjusted regression coefficients (95% confidence interval if calculated)		
			age	male (female as a referent)	hair mercury concentration ≥ 50 ppm (< 50 ppm as a referent)
cranial nerve	sensorineural hearing loss	logistic regression	1.05 (1.00, 1.10) *	1.62 (0.46, 5.74)	7.80 (1.88, 32.29) **
muscular weakness	upper limb	logistic regression	0.97 (0.91, 1.04)	0.22 (0.02, 2.30)	$6.49x10^{6}$ (-)
	lower limb	logistic regression	1.04 (0.94, 1.14)	0.15 (0.01, 1.60)	$2.49x10^{6}$ (-)
tremor	postural	logistic regression	1.12 (1.04, 1.20) **	1.24 (0.32, 4.79)	$6.97x10^{6}$ (-)
coordinated movement	diadocho - kinesis	logistic regression	1.21 (1.02, 1.43) *	1.70 (0.15, 19.3)	$1.98x10^{7}$ (-)
	finger-to-nose test	logistic regression	1.17 (0.99, 1.39)	$2.85x10^{7}$ (-)	$2.07x10^{6}$ (-)
	heel-knee test	logistic regression	1.12 (1.03, 1.22) **	4.65 (0.52, 41.7)	$9.20x10^{6}$ (-)
	knee tapping test	logistic regression	1.11 (0.99, 1.24)	$4.76x10^{7}$ (-)	$1.40x10^{6}$ (-)
one foot standing	right foot < 5s	logistic regression	1.13 (1.02, 1.24) *	1.32 (0.022, 7.94)	$1.20x10^{6}$ (-)
	right foot < 15s	logistic regression	1.11 (1.07, 1.16) ***	0.81 (0.34, 1.92)	1.02 (0.24, 4.28)
	left foot < 5s	logistic regression	1.11 (1.03, 1.19) **	0.96 (0.23, 4.06)	$1.04x10^{6}$ (-)
	left foot < 15s	logistic regression	1.13 (1.08, 1.18) ***	1.00 (0.42, 2.40)	0.88 (0.20, 3.84)
simple gait		logistic regression	1.10 (0.99, 1.22)	1.90 (0.19, 19.3)	10.21 (1.29, 80.56) *
tandem gait		logistic regression	1.31 (1.03, 1.68) *	$2.22x10^{7}$ (-)	$1.88x10^{6}$ (-)

reflex	upper limb	logistic regression	1.05 (1.02, 1.08) **	3.21 (1.40, 7.35) **	0.42 (0.09, 2.10)
	lower limb	logistic regression	1.06 (1.02, 1.09) ***	1.72 (0.79, 3.76)	1.37 (0.38, 4.99)
	Babinski	logistic regression	1.13 (0.99, 1.29)	0.56 (0.07, 4.82)	$3.03x10^{6}$ (-)
	Chaddock	logistic regression	1.13 (0.99, 1.29)	0.56 (0.07, 4.87)	$3.03x10^{6}$ (-)
touch sensation		logistic regression	1.07 (1.02, 1.12) **	1.62 (0.55, 4.82)	0.64 (0.08, 5.47)
pain sensation		logistic regression	1.06 (1.02, 1.10) **	1.10 (0.42, 2.84)	0.55 (0.07, 4.61)
vibratory sense	right upper limb (s)	linear regression	-0.093 (-0.12, -0.063) ***	0.14 (-0.76, 1.03)	-0.10 (-1.89, 1.64)
	left upper limb (s)	linear regression	-0.086 (-0.11, -0.060) ***	-0.099 (-0.91, 0.71)	-0.33 (-1.96, 1.29)
	right lower limb (s)	linear regression	-0.15 (-0.18, -0.13) ***	0.33 (-0.47, 1.13)	-0.84 (-2.44, 0.76)
	left lower limb (s)	linear regression	-0.15 (-0.18, -0.13) ***	-0.002 (-0.77, 0.77)	-0.62 (-2.15, 0.92)
two-point discrimination	right index finger (mm)	linear regression	0.019 (0.002, 0.037) *	-0.34 (-0.86, 0.18)	-0.20 (-1.24, 0.84)
	left index finger (mm)	linear regression	0.024 (0.004, 0.044) *	-0.22 (-0.82, 0.39)	-0.08 (-1.29, 1.13)
graphesthesia	right palm (/4)	linear regression	-0.001 (-0.002, 0.001)	-0.006 (-0.042, 0.031)	0.024 (-0.050, 0.098)
	left palm (/4)	linear regression	-0.001 (-0.003, 0.001)	0.038 (-0.022, 0.098)	0.038 (-0.082, 0.159)
stereognosis (/3)		linear regression	-0.001 (-0.002, 0.000)	-0.022 (-0.052, 0.008)	0.018 (-0.042, 0.079)

Summary of neurological findings of 12 residents whose hair mercury concentrations were over 50 ppm

No	sex	hair mercury (ppm)	wide-based gait	sensorineural hearing loss	cerebellar sign	sensory disturbance and two-point discrimination (mm)
1	M	50.4	(-)	(-)	(-)	(-) two-point discrimination: 6.0, 6.0
2	M	50.6	mild (+)	(-)	(-)	reduced vibratory sense of the lower limbs: 5s, 4s two-point discrimination: 2.0, 2.6
3	M	54.0	(-)	left (+)	(-)	(-) two-point discrimination: 1.5, 1.5
4	M	59.2	(+)	(+)	(-)	(-) two-point discrimination: 2.1, 2.1
5	M	59.2	(-)	(-)	(-)	(-) two-point discrimination: 4.0, 5.0
6	M	65.0	(-)	(-)	(-)	(-) two-point discrimination: 2.5, 3.3
7	M	66.2	(-)	(+)	(-)	(-) two-point discrimination: 5.0, 4.2
8	M	68.4	(-)	(+)	(-)	dysesthesia (left L5, S1) two-point discrimination: 3.2, 3.8
9	F	72.2	(-)	(-)	(-)	reduced vibratory sense of the lower limbs: 5s, 5s two-point discrimination: 5.0, 5.0
10	F	73.1	(-)	(-)	(-)	(-) two-point discrimination: 3.8, 3.8
11	M	82.6	(-)	(-)	(-)	(-) two-point discrimination: 2.6, 2.2
12	M	101.9	(-)	(-)	(-)	reduced vibratory sense of the lower limbs: 6s, 7s two-point discrimination: 2.7, 3.5

Conclusion

1. The hair mercury level in Taiji residents was markedly higher than that in other areas of Japan.

2. Although detailed clinical neurological examinations showed several clinical findings in some residents, they were not due to MeHg exposure but other neurological causes.

3. Multivariable analytical study demonstrated that there were no significant correlations between hair mercury concentrations and neurological outcomes, while some of the findings were correlated with ages.

Collaborators

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