APPLICATION OF PSYCHOPHYSICS TO THE EXPLORATION OF MINAMATA DISEASE (METHYLMERCURY POISONING), WHICH DISTURBS SENSORY CORTEX

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Abstract

Minamata disease (MD), a methylmercury poisoning from fish and shellfish contaminated by Chisso Company waste discharge, was found in 1956. Small input neurons of the cerebral cortex in the fourth layer including somatic, visual, auditory, tasting, and olfactory areas are destroyed in MD. Several ten thousand people were suffered from MD in the polluted area. But socio-economical environment, discrimination against MD patients, and the lack of the disease information concealed the vast spread of MD. Somatosensory disturbance is the main symptom of MD, but it has been ignored by the Government and so-called specialists for a long time. We have been succeeding in measuring sensory acuity by using psychophysical methods using fine abrasive papers and other quantitative methods. We would like to introduce these studies and discuss further exploration of other ways of studying cortical sensory systems.

Background

Minamata disease (MD) is a methylmercury poisoning from fish and shellfish. The Chisso Company in Minamata began to use mercury as a catalyst in the production of acetaldehyde in 1932, and discharged mercury to the sea. MD was discovered in 1956. The most severe symptoms of MD are known as Hunter-Russell syndrome, which is consisted of somatosensory disturbance, motor ataxia, visual constriction, hearing disturbance, and dysarthria. The Japanese Government permitted the Chisso Company to discharge the mercury even after the discovery of severe illness. In 1968, 13 years after the discovery, several months after the Chisso Company finished the acetaldehyde production, the Japanese Government admitted MD as a methylmercury poisoning for the first time (Fig. 2). For more than 30 years, residents living along the coast of Yatsushiro Sea (Shiranui Sea) continued eating contaminated fish and shellfish.

The pollution spread along all the coasts of Yatsushiro Sea (Fig. 1). About 2000 patients have been certified as MD in this area. But in order to be certified as MD, patients must have sensory disturbance and other symptoms like cerebellar ataxia or visual constriction. About two hundred thousands people are living in the polluted area. There thought to be several ten thousands residents who have affected by methylmercury even now.

In 1995, over 10,000 patients were partially compensated for their health problem including somatosensory disturbance, but they were not certified as MD. Many residents and MD patients have experienced severe social discrimination in the region and they could not propose aid for their health problem. After the judgment of Supreme Court in October 2004, which admitted the responsibility of the Japanese Government for spreading MD, more than 15,000 residents newly began to receive physical examination for MD. We have examined more than 3,800 residents.

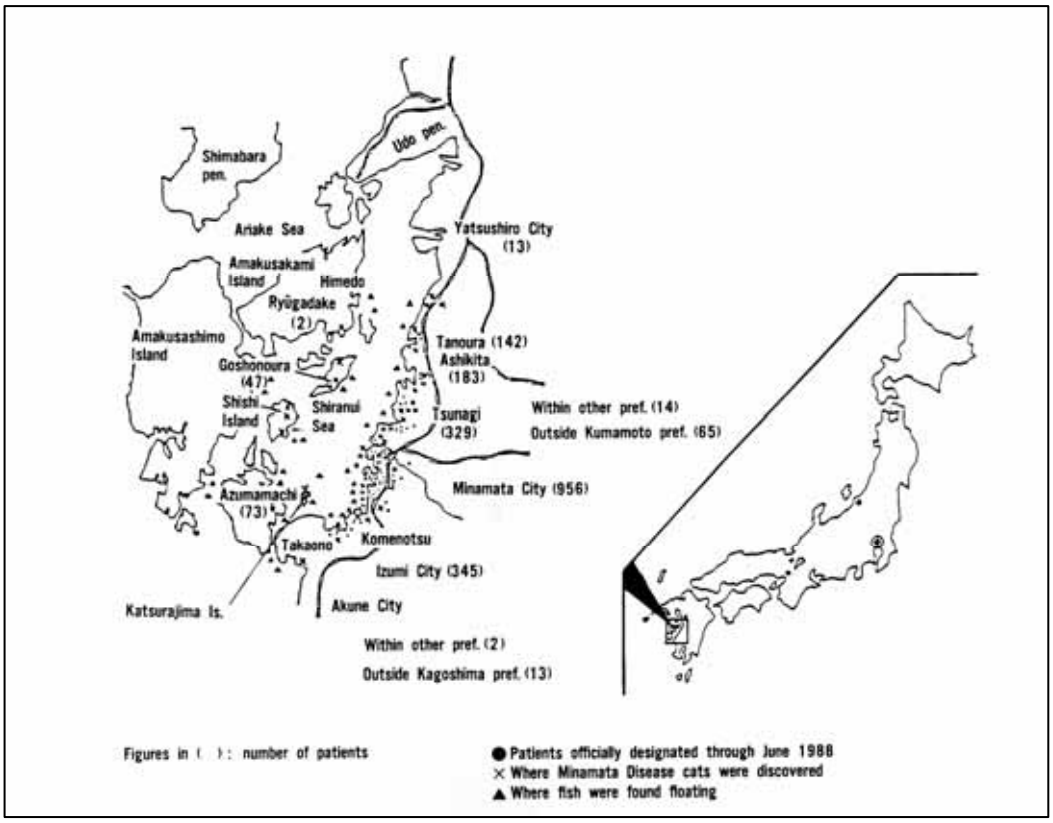

Fig. 1. Yatsushiro (Shiranui) Sea and Spread of Contamination

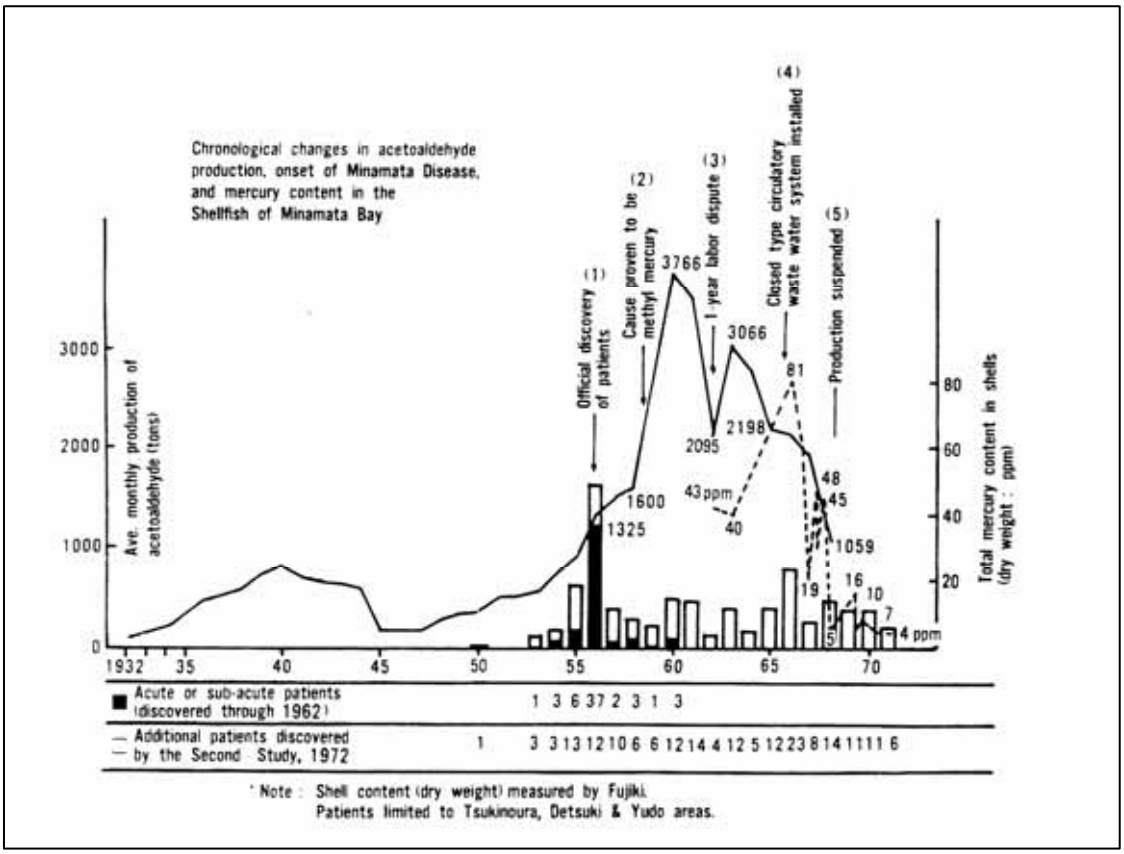

Fig. 2. History of Acetaldehyde Production and Pollution in Nature and to Human

Complaints of Minamata disease and their responsible organ

The most prevalent complaint of adult type MD is somatosensory disturbance. It began from the peripheral parts of four limbs, and some patients complain disturbance around mouth. Patients also experience ataxias, auditory disturbance, dysarthria, and constriction of visual field. Tasting or olfactory disturbance can occur in many cases, but there are few studies which treat them. The more MD becomes serious, the more the complaints and symptoms increase.

In Japan, somatosensory disturbance was supposed to be caused by polyneuropathy, in which glove and stocking type sensory disturbance is observed. But nowadays, the sensory disturbance in MD has been supposed to be caused by cortical injury and it can show cortical character. Some patients can hear voice but cannot understand the correct meaning of it. Deep tendon reflex are kept normal, and there are no correlations between somatosensory acuities and sensory nerve conduction velocities.

Methylmercury injures small neurons of the central nervous system (CNS). Especially, neurons in the fourth layer of the cerebral cortex including postcentral (parietal) and calcarine (occipital) which receive input fibers from thalamus, and granular cells in the cerebellum are vulnerable. Although ataxias of MD have been supposed to be caused by cerebellar dysfunction, sensory ataxias are more observed in the chronic MD.

The symptoms of fetal type MD are quite different from those of adult type. In fetal type MD, the whole CNS is vulnerable, not restricted within the special regions of the CNS like adult type. Their main symptoms are prominent motor disturbance (including dyskinesia, posture abnormalities, and dysarthria), visual, auditory abnormalities. They are similar to cerebral palsy. Interestingly, there are some fetal type MD patients not necessarily with distinct somatosensory disturbance.

Psychophysical Somatosensory Measurement

Sensory disturbances can be measured by quantitative methods. There were some reports which described the two-point discrimination threshold in the methylmercury-polluted area. However, there were no psychophysical quantitative methods. We measured fine-surface-texture discrimination; one sub-modality of tactile sensation, by psychophysical methods in subjects believed to have been exposed to the pollution for the first time and compared their findings to those of healthy individuals who denied any possibility of exposure.

Four groups of subjects from 60 to 79 years of age were studied between August 2000 and August 2001 (Table 1). Aluminum-oxide abrasive papers were used as stimuli. Difference thresholds from 3μm were calculated by the two-alternative, forced-choice technique. The stimuli used were six aluminum-oxide abrasive papers (Sumitomo 3-M). These abrasive papers were the same as ones used by Miyaoka *et al* (1999). Average particle sizes of the papers were 30, 12, 9, 5, 3, and 1μm. The abrasive papers were cut into 5 x 5cm-squares.

Table 1. Background of Subjects

	Age	Number	Sex (M/F)	Fisherman's Family
Control Subjects	70.0 +- 5.5	27	12 / 15	0%
Exposed Subjects without Numbness	69.8 +- 5.5	17	7 / 10	18%
Exposed Subjects with Numbness	69.1 +- 4.5	23	9 / 14	61%
Certified Subjects with Numbness	69.7 +- 5.3	13	8 / 5	100%

Subjects were seated in a chair and wore a mask. The method of constant stimuli was used. They touched two stimuli with the index finger of the dominant hand, and determined which abrasive paper felt rougher using the two-alternative, forced-choice technique. The standard stimulus was 3μm. The combinations of stimuli were 30 vs. 3μm, 12 vs. 3μm, 9 vs. 3μm, 5 vs. 3μm, 3 vs. 3μm, and 1 vs. 3μm.

Each subject completed ten discrimination trials for each stimulus combination. Randomized 60 experimental trials were performed for each subject. The temperature of the stimulated skin of subjects was maintained at greater than 30 degrees.

The difference threshold was (1) 6.2μm, (2) 6.4μm, (3) 4.9μm, and (4) 2.7μm and the psychometric function is shown in Fig. 3. We found the fine-surface-texture discrimination was the same between certified and non-certified exposed subjects. There is a clear difference between these subjects and control subjects. Furthermore, subjects from the Minamata area without complaints of numbness or neurological deficits by conventional examination had a mild disturbance of fine-surface-texture discrimination. These findings suggest that methylmercury exposure in the past in this population may have been more extensive than previously reported.

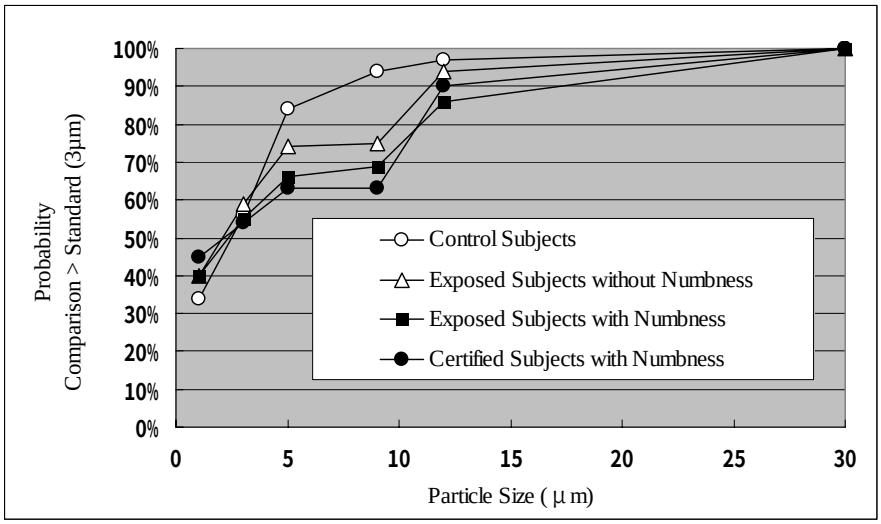

Fig. 3. Psychometric Function of Fine-Surface-Texture Discrimination of Index Finger

Quantification of Other Somatosensory Modalities

Following the determination of the Supreme Court of Japan in October 2004, we newly examined residents. Until April 2005, we studied 197 residents from the Minamata area who had a history of fish consumption during the polluted period to determine the importance of sensory symptoms and findings in making a diagnosis of MD. We divided the exposed subjects into non-complicated (Group E: n=74, Age=61.4+-10.6) and complicated (Group E+N: n=74, Age=62.4+-8.6) groups based on the absence or presence of other neurological or neurologically related disorders and compared them to residents in control area (Group C: n=111, Age=61.9+-9.9) after matching for age and sex.

We quantitatively measured four somatosensory modalities and did psychophysical tests of fine-surface-texture discrimination of the right index finger. Four modalities consist of minimal tactile sense by Semmes-Weinstein monofilaments (6 portions of body), vibration sense (5), position sense (4), and two-point discrimination (3). Minimal tactile sense was measured by 20 kinds of Semmes-Weinstein monofilaments. Each monofilament was tested once in general and tested by answering yes when the subject can sense. Vibration sense was measured by 125 Hz tuning fork and stopwatch. Position sense

was measured by using a rular. The interval distance was 5mm, and the minimum distance was 5mm. The distances tested were 1, 2, 3, 4, 5, 6, 8, 10, 12, 15, 20, 25, 30, and 36mm for the two-point discrimination with a drafting divider. Thresholds were measured by a rular with 3 times two-alternative, forced-choice test.

Fig. 4-9 are based on the data of the right wrist of the vibration sense and of the right index finger of the other senses. All sensory modalities were impaired in the E and E+N groups (Fig. 4-7). All four quantitatively measured sensory modalities were correlated. Fine-surface-texture discrimination were also disturbed (Fig. 8-9). There were almost no correlations between these sensory acuities and the median sensory nerve conduction velocity. We concluded that sensory symptoms and findings are important in making the diagnosis of MD.

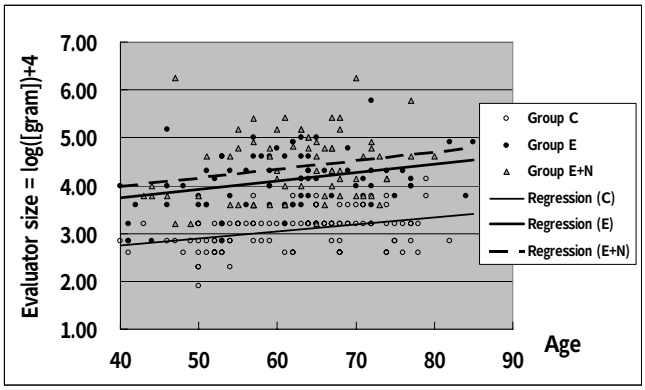

Fig. 4. Minimal Tactile Sense

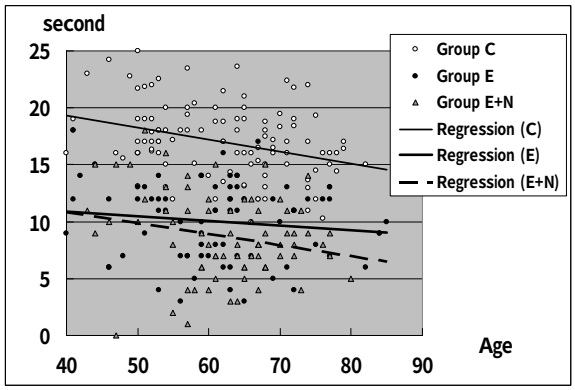

Fig. 5. Vibration Sense

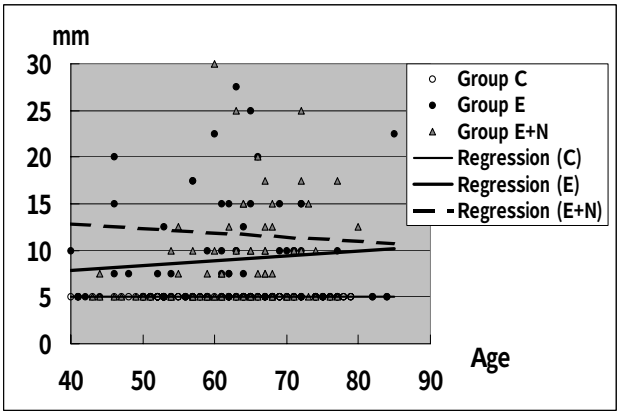

Fig. 6. Position Sense

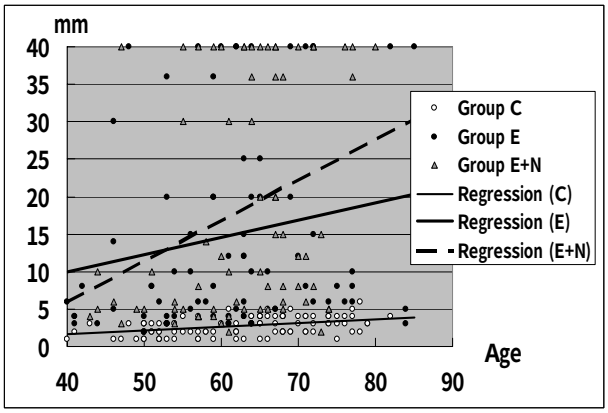

Fig. 7. Two-Point Discrimination

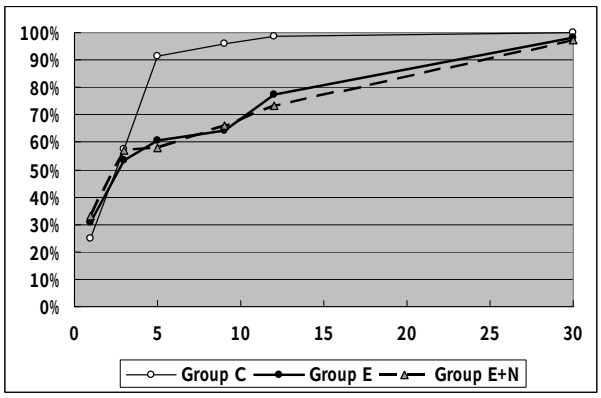

Fig. 8. Texture Discrimination (Age 40-59)

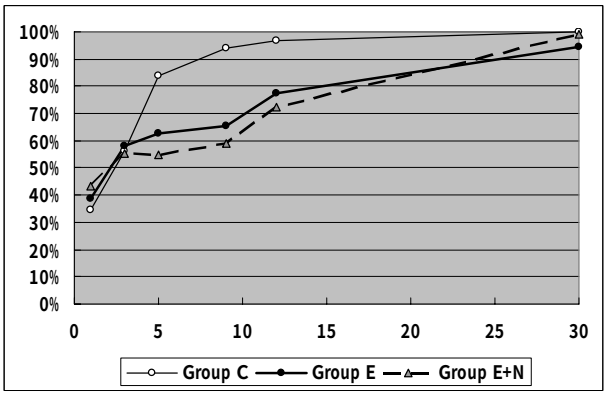

Fig. 9. Texture Discrimination (Age 60-79)

Other Subjects Remained Unsolved

Unfortunately, MD was caused by a company whose development was closely related with national policy. So the company and the Government had enough motivation to conceal this disease, and some medical specialist co-operated the Government by making the medical criteria of MD strict without medical evidence. The regional discriminations against patients were left and medical professionals often interpreted the complaints of patients as “conversion reaction” or “malingering” without precise examinations or studies. Are there any psychophysical data that are related to conversion reaction or malingering?

In MD, symptoms have fluctuations in some cases. It might be a characteristic of the cortical disturbances. In some cases, psychological tensions seem to cause such fluctuations. Studying relations between sensory acuities and psychological tensions might be helpful for studying fluctuation. How can we measure them?

The cerebral cortex has plasticity. Because the sensory acuity of MD has not been measured quantitatively and chronologically, we have not obtained information about functional plasticity of MD. If the injury by methylmercury is mild, the function can be better. Such clinical observations were reported, but there were no precise data. On treating fluctuation, we have to confront the problem as follows: the fluctuations are based both on organic plasticity and on functional factors. How can we answer to this problem?

The reason why distinct somatosensory disturbance in the fetal type MD is slighter is unsolved. Such dissociation is also observed in SMON disease that is caused myelopathy by quinoform. How can the dissociation of sensory disturbance between fetal and adult type be caused? Is it related to the development of the CNS?

MD disturbs not only the somatosensory system, but also visual, auditory, tasting, and olfactory systems. But psychophysical technique has not been applied enough to MD research in such systems. What kind of psychophysical technique can be used for MD research? Furthermore, effects of methylmercury on mentality and intellects are known.

Adult type MD is a rare disease in which sensory related neurons in the CNS are selectively injured. We would like to continue quantitative and psychophysical study of methylmercury intoxication with both views of proving the sensory disturbances of MD and exploring sensory mechanism of CNS.

Acknowledgements

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