Chronic elemental mercury intoxication: neuropsychological follow-up case study

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(Received 25 May 1995; accepted 1 August 1995)

In initial and follow-up investigations of neuropsychological function in a patient with elemental mercury intoxication, his scores were compared with those of a group of normal control subjects matched for sex, age and education. Each subject received a comprehensive neuropsychological examination including a personality inventory. On the initial examination the results indicated that the patient had a significant depression of performance intellectual functioning, impairments of attention, non-verbal short-term memory and visual judgement of angles and directions, psychomotor retardation and personality changes including depression, anxiety, desire to be alone, lack of interest and sensitivity to physical problems. Such an impairment picture is compatible with the previous observations of individuals with chronic exposure to elemental, organic or inorganic mercury. The follow-up study was undertaken about 1.5 years later. The results show that the patient's cognitive and personality functions were fully recovered. Our findings thus suggest a reversibility of impaired neuropsychological function in persons with elemental mercury poisoning if a prompt removal from the toxic environment is accomplished, together with proper medical treatment.

Introduction

Occupational exposure to mercury has been reported in miners, furcutters, mirror makers, gilders, hatters, dentists, and manufacturers of chlorine, chloralkali, thermometers, lamps, and thermonuclear weapons [1,2]. Neurotoxic effects of chronic exposure to mercury are well known. Generally, neuropathological changes in humans have been found in frontal and occipital cortices, basal ganglia, substantia nigra, superior temporal cortex, cerebellum, and subcortical white matter [3-6]. Grandjean [5] claimed that lesions resulting from elemental mercury intoxication were located in the occipital cortex and substantia nigra. Neurological deficits due to organic type poisoning include severe encephalopathy with persistent neurological disabilities [7] or a syndrome comparable to amyotrophic lateral sclerosis [8,9], while inorganic or elemental mercury intoxication can produce polyneuropathy and tremor, and may further result in decreased visual acuity, particularly for night vision, slurred speech, disturbance of equilibrium, intention tremor, ataxic gait, and involuntary jerky movements if the disease progresses [10-12]. Neuropsychiatric problems due to inorganic mercury exposure include avoidant, irritable and overly sensitive interpersonal behaviour; depression; lassitude and

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fatigue [13]. The term 'erethism' has been used to refer to such a constellation of emotional disturbances [2]. Neuropsychological impairments mainly involving defects of visual-motor coordination, abstract reasoning and memory, especially non-verbal short-term memory, and visuospatial abilities, have also been reported [13-15]. However, most of these cognitive and emotional problems were found in patients exposed to inorganic or organic, rather than elemental, mercury. Although there are a few studies [16,17] of persons exposed to elemental mercury, overall there is a paucity of information regarding the effects of such exposure on cognitive and emotional functions. Furthermore, there have been few longitudinal studies of neuropsychological consequences of chronic exposure to elemental mercury, and the reversibility of neurobehavioural changes after such chemical poisoning is as yet unclear, so in the present study we made an attempt to investigate these matters using a longitudinal approach.

Materials and methods

On 5 August 1991, a 29-year-old male with a 12th-grade education, who worked in a lampsocket manufacturing factory in northern Taiwan, complained of tremor and unsteady gait, for 4 months. He had suffered from severe gum pain, loss of body weight, general malaise and emotional instability for 2 years. Gingivitis, and prominent sweating on the palms and soles, were noted. Neurological examination showed a mild constriction of visual fields, slurred speech, prominent dysidiadochokinesia, dysmetria, dysnergia, postural and action tremor of both hands, and ataxic gait. The patient could not perform Tandem's walk. Laboratory tests revealed a normal haemogram, biochemistry, EEG, EKG, evoke potentials, chest radiography, brain CT and MRI. However, the mercury concentration was 237 $\mu\text{g/l}$ in blood and 610 $\mu\text{g/l}$ in 24-h urine. The patient received D-penicillamine 150 mg per day for 1 week and then 300 mg per day for 7 weeks, and was followed in the out-patients department for 2 years. His gait problem improved, and disappeared 2 months later. The improvement of action tremor was slower and the condition took 4 months to abate. With D-penicillamine treatment, blood mercury concentrations showed a rapid decrease in the first 2 weeks, and then slowly returned to normal in the next 8 weeks. Monitoring of 24-h urinary mercury showed an increase in the first week and a slow decrease within 2 months. The clinical summary has been reported elsewhere [18]. The patient received a comprehensive neuropsychological examination at the Neuropsychology Laboratory, Department of Neurology, Chang Guang Memorial Hospital, Taipei on 11 August 1991, and a follow-up study on 5 March 1993 after cessation of exposure for about 1.5 years.

Thirty normal, healthy subjects, randomly selected volunteers and matched for sex, age and educational level in years with the patient, served as controls. Each subject also received a comprehensive neuropsychological examination at the Neuropsychology Laboratory, Department of Neurology, Chung Gung Memorial Hospital, Taipei on 11 August 1991. The tests, covering orientation, learning and memory, intelligence, language and communication, spatial perception, visual perception, visual attention, manual dexterity, information processing speed, and personality are as follows:

Orientation: Temporal Orientation (TO) [19] and Orientation to Personal Information and Place (OPIP) [20]; verbal learning and short-term memory: Serial Digit Learning (SRL) [19] and Word Sequence Learning (WSL) [21]; non-

Table 1. Demographic characteristics of subject groups

	Age (years)			Education (years)			n
	Mean	SD	Range	Mean	SD	Range	
Patient	29	n.a.	n.a.	12	n.a.	n.a.	1
Normals	28.33	3.48	20–36	11.50	1.96	9–14	30

n.a. = Not available.

verbal learning and short-term memory: Benton Visual Retention Test (BVRT) [22] and Continuous Recognition Memory (CRM) [23]; intellectual function: WAIS-R [24]; language and communication: Multilingual Aphasia Examination (MAE) [25] including Visual Naming (VN), Semantic Verbal Fluency (VF), Token Test (TT), Aural Comprehension (AC), Oral Reading (OR), Reading Comprehension (RC), Spontaneous Story Writing (SS), Spontaneous Writing of Name and Address (NA), Spontaneous Writing of Words and Phrases (SW), Writing to Dictation of Words (DW), Writing to Dictation of Sentences (DS), Writing from Copy of Words (CW) and Writing to Copy of Sentences (CS); spatial perception: Judgement of Line Orientation (JLO) [19] and Three-Dimensional Block Constructional-model (3-DBC) [19]; visual perception: Facial Recognition Test (FRT) [19] and Visual Form Discrimination (VFD) [19]; visual attention: Line Cancellation Test (LCT) [26], and Gordon Diagnostic System (GDS) [27], including a 6-min vigilance and distractibility subtest; manual dexterity and psychomotor function: Purdue Pegboard (PP) [28] and Finger Tapping Test (FT) [29]; information processing speed: Paced Auditory Serial Addition Task-Revised (PASAT-R) [30]; frontal function: Wisconsin Card Sorting Test-Short Form (WCST-S) [31]; personality function: Ko’s Mental Health Questionnaire (KMHQ) [32], which is a self-report (true and false) format with a total of 282 items including 11 scales. These scales are Paranoia (KPa), Hypochondriasis (KHs), Psychopathic deviate (KPd), Self-Confidence (KSc), Inferiority (KI), Anxiety/Psychasthenia (KAp), Compulsiveness (KC), Sexual Suppression (KSs), Aggression (KAg), Self-Awareness/Ego Strength (KEs), and Independence (KIId). A high score on the scales of KPa, KHs, KPd, KI, KAp, KC, KSs, and KAg indicates psychopathology, and a high score on the scales of KSc, KEs and KIId reflects normal personality functioning. With regard to the instructions and scorings of these tests, please refer to the references. Before receiving the neuropsychological examination each subject was given written informed consent. A total of 3 h was needed for each subject to complete the testing in one session.

Results

For most of the neuropsychological measures the patient’s test score was considered abnormal when it was 1.5 standard deviation below the mean score of the normal control group, while for the temporal orientation and the error score of the BVRT, an impaired score was defined as a score 1.5 standard deviation above the mean error score of the nominal control group. An impaired score on the scales of KPa, KHs, KPd, KI, KAp, KC, KSs and KAg of KMHQ was defined as the test score 1.5 standard deviation above the mean score of the normal control group, while a detective score on scales of KSc, KEs, and KIId was 1.5 standard deviation below

Table 2. Comparisons of test results of orientation, learning and memory, and intelligence between normals and patient

	Normals (<i>n</i> = 30)		Patient (<i>n</i> = 1)	
	Mean	SD	1991	1993
Orientation				
TO	0·3	0·53	0	0
OPIP	11·6	0·62	12	12
Intellectual functioning				
WAIS-R				
VIQ	104·93	14·83	105	109
PIQ	95·17	12·52	73†	93
FSIQ	101·03	14·00	91	103
Verbal learning and memory				
SDL-12	13·60	7·52	14	19
WSL				
Short-term memory	53·27	5·69	46	59
10-minute recall	4·73	1·28	6	6
Non-verbal learning and memory				
BVRT				
Correct	8·17	1·05	3†	9
Error	2·27	1·44	14†	1
CRM				
Hit	37·03	2·31	34	36
False alarm	12·57	11·06	11	13
Total correct	86·70	6·98	83	83

† Defective performance.

the mean score of the normal control group. Tables 2–5 indicate the results. On the first neuropsychological examination the defective test scores include the PIQ of the WAIS-R, both correct and error scores of BVRT, JLO, both of correct and time scores of 3-DBC, the time score of LCT, both of omission and correct scores of vigilance and distractibility, Purdue Pegboard, Finger Tapping Tests, the first subtest (2·8 s) and total correct scores of PASAT-R. With regard to personality functioning, the elevated scores were evident on the KMHQ's scales of KHs, KPd, KI, KAp and KAg. Normal cognitive and personality functions, however, were shown in the follow-up study.

Discussion

On the first examination our patient manifested cognitive impairments including performance intellectual functioning, non-verbal short-term memory, visuospatial perception, visually sustained and selective attention, manual dexterity, information processing and psychomotor speed. These cognitive changes, especially for deficits of manual dexterity and psychomotor speed, however, might be partially due to the patient's tremor problem. Meanwhile, the patient showed some personality changes with depression, anxiety, desire to be alone, lack of interest, and hypochondriacal tendency. Since the patient was very cooperative during the time period of receiving neuropsychological examination, such personality changes seemed less likely to be secondary to his illness symptoms, such as general malaise. The non-verbal short-

Table 3. Comparisons of test results of language, spatial perception, and visual perception between normals and patient

	Normals (n = 30)		Patient (n = 1)	
	Mean	SD	1991	1993
Language and communication				
MAE				
VN	54.27	3.78	56	60
SR	12.20	1.19	n.a.	14
VF	36.60	6.61	35	41
TT	42.83	1.23	40	42
AC	17.73	0.52	16	18
OR	17.63	0.49	18	18
RC	17.57	0.50	17	17
SS	29.17	8.48	19	33
NA	17.27	0.58	18	18
SW	12.07	3.43	12.5	15
DW	9.80	1.81	10.5	11
DS	12.47	0.82	13	13
CW	15.70	0.54	n.a.	16
CS	10.97	0.18	n.a.	11
Spatial perception				
JLO	23.43	3.74	16†	25
3-DBC				
Correct	28.80	0.61	29	29
Time(s)	86.80	25.27	139 ^{##} †	70 ^{##}
Visual perception				
FR T	45.87	4.74	49	41
VFD	29.47	2.57	30	32

n.a. = Not available.
† Defective performance.

term memory and psychomotor problems evident in our patient due to chronic elemental mercury poisoning are respectively consistent with the observations of Smith and colleagues [17], and Langolf and co-workers [16]. The non-verbal short-term memory problem of our patient was mainly reflected by his impaired performance on the Benton Visual Retention Test, which can also be used to measure immediate visual attention span [33]. Whether such a non-verbal short-term memory problem in our patient was secondary to his visual attention dysfunction is not known. If this is the case, the inclusion of measures of visually sustained and selective attention in a comprehensive neuropsychological test battery for examining workers or patients chronically exposed to elemental mercury might be necessary. Overall, the cognitive impairment picture of our patient is similar to that of workers or patients resulting from inorganic mercury intoxication [13–15]. Also, the findings of personality changes in our patient derived from the objective personality inventory plus the indirect evidence of irritability at home reported by his spouse seemed to further support the previous observations [2,13]

About 1.5 years after discontinuing exposure and receiving D-penicillamine treatment, the patient was re-examined with the same tests. The results indicated that both cognitive and emotional functions were back to normal. In a review

Table 4. Comparisons of test results of visual attention, manual dexterity, and information processing speed between normals and patient

	Normals (n = 30)		Patient (n = 1)	
	Mean	SD	1991	1993
Visual attention				
LCT				
Right visual field	30*00	0*00	30	30
Left visual field	29*87	0*35	30	30
Total correct	89*83	0*38	90	90
Time (s)	51*27	23*87	105 [†]	45 [†]
GDS				
Vigilance (6 min)				
Commission	1*27	2*60	2	1
Omission	0*80	1*37	5 [†]	1
Correct	29*20	1*37	25 [†]	30
Distractibility (6 min)				
Commission	4*70	11*83	5	3
Omission	4*77	5*88	14 [†]	1
Correct	25*30	5*27	17 [†]	29
Manual dexterity				
PP				
Dominant hand	16*43	1*41	6 [†]	15
Non-dominant hand	15*13	1*38	5 [†]	13
Both hands	13*10	1*32	5 [†]	12
FT				
Dominant hand	59*00	10*44	24 [†]	56
Non-dominant hand	52*20	8*68	28 [†]	59
Information processing speed				
PASAT-R				
ISI (2*8 s)	22*90	3*16	16 [†]	23
ISI (2*4 s)	22*37	3*32	18	23
ISI (2*0 s)	22*90	4*40	15	25
ISI (1*6 s)	20*20	5*12	14	22
Total correct	85*87	14*76	63 [†]	93

[†]Defective performance.

article, Hänninen [13], based on a series of cross-sectional study findings of her research team and other investigators, has addressed the issue of reversibility of motor and cognitive impairments, and emotional disturbances in workers due to chronic elemental, inorganic or organic mercury exposure. She claimed that motor problems are more reversible than cognitive and emotional changes because motor symptoms are easily identified and more often lead to cessation of exposure, which is not the case for workers with cognitive and emotional changes. In her view, the chance for cognitive and emotional function recovery is not high. Our findings, however, did not seem to support Hänninen's notion. The difference might be due to: (1) our findings derived from a follow-up case, rather than a cross-sectional type of research design; and (2) our subject was a patient with elemental mercury intoxication having neurological problems, rather than the workers exposed to elemental, inorganic, or organic mercury who did not manifest neurological symptoms. Future investigation of this issue is needed.

Table 5. Comparisons of test results of frontal functioning and personality functioning between normals and patient

	Normals (n = 30)		Patient (n = 1)	
	Mean	SD	1991	1993
Frontal functioning				
WCST				
No. of complete categories	5.53	1.66	6	7
No. of perseverative errors	2.50	2.45	3	1
No. of non-perseverative errors	6.73	4.25	4	5
No. of unique errors	1.27	2.52	1	0
Personality functioning				
KMHO				
KPa	6.33	2.88	6	2
KHs	6.77	3.64	14†	7
KPd	6.33	3.85	12†	6
KSc	8.50	2.84	8	6
KI	6.20	3.78	12†	4
KAp	5.17	4.33	17†	1
KC	8.77	4.20	14	8
KSs	10.73	2.85	7	12
KAg	5.97	3.94	14†	6
KEs	17.10	8.88	16	16
KId	15.70	3.61	16	17

†Defective performance.

In summary, this is the first follow-up case study to explore the issue of the reversibility of cognitive and emotional impairments in a patient with chronic elemental mercury intoxication. The general impairment picture from the initial neuropsychological examination seems to corroborate earlier findings in patients suffering with elemental, inorganic or organic mercury intoxication. A follow-up study of our patient shows a full recovery of both cognitive and emotional functions, suggesting a better prognosis in chemical elemental mercury intoxication than organic mercury intoxication. We further emphasized that the early removal from the exposure and early treatment might prevent the sequelae of cognitive and emotional alternations in patients with chronic elemental mercury intoxication.

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