

SHORT REPORT

Neuropsychology of thallium poisoning

T M McMillan, R R Jacobson, M Gross

Abstract

Cases of thallium poisoning are rare and neuropsychological assessment has only been reported in detail in one other case. In the case reported here, neuropsychological assessments were carried out three, 12, and 54 months after diagnosis of thallium poisoning in a man who had acutely shown a number of neurological signs including confusion and disorientation and generalised slowing of EEG which was more prominent on the left. Evidence suggested that he had been exposed to thallium over a period of weeks. Neuropsychological assessment indicated an unexpected weakness in verbal abilities which persisted. This finding is consistent with the only other published case report which details neuropsychological effects after a single large dose of thallium and which also found a lateralised impairment.

(*J Neurol Neurosurg Psychiatry* 1997;63:247-250)

Keywords: neuropsychology; thallium poisoning

Thallium is present in very low concentrations in the environment.¹ Poisoning is rare and it is usually found in the context of suicide or homicide²⁻⁶ or after accidental exposure if entering the food chain via rodenticides or insecticides.^{7,8} Thallium is used in industrial settings¹ but here exposure is usually less severe.⁹ It is a neurotoxin, producing painful peripheral neuropathy, which is one of two cardinal symptoms (the other being alopecia). In addition it can cause ataxia, tremor, athetosis, and cranial nerve palsies, and can lead to coma, convulsions, and death.¹⁰ It can cause abnormal slowing on EEG usually without focal or lateralising features.^{4,8,11-13} Normal EEGs have been found in most but not all reported cases who remained alert and oriented.^{2,4} In one case diffuse slowing, especially in the occipital region, was reported.¹¹ Neuropathological studies have disclosed cerebral cortical, subcortical, and brain stem damage.^{14,15} Brain scans are often normal.¹⁶

Acute agitation and aggression have been reported¹³ as have personality change, depression, poor self care, insomnia, apathy, and confabulation in adults^{2,4,5,17,18} and persisting "re-

tardation and psychosis" in adults and in children.^{8,19} These psychiatric symptoms can occur in cases with or without psychiatric history and anxiety and insomnia would seem to be most often described.

This paper describes the postacute and follow up neuropsychological testing of a single case, there being only one further published case in which such investigations are reported in detail.¹³

Subjects and methods**HISTORY OF THE CONDITION**

In early December, 1991 a 44 year old right handed man was admitted to his local district general hospital with chest pain, which was investigated and thought to be caused by hiatus hernia. He was readmitted three weeks later with a two week history of general malaise and feeling unsteady. He had developed a pustular rash, especially on his legs and hands. He became increasingly confused and disoriented with vomiting and was admitted as an emergency to the department of neurology at Atkinson Morley's Hospital in early January 1992.

On admission he was confused and disoriented, had pronounced alopecia, had a purplish rash on hands and fingers, and was afebrile. He had bilateral horizontal nystagmus, bilateral lower motor neuron facial weakness, and global weakness of his limbs, especially proximally. Coordination was slow but accurate, vibration and joint position senses were globally reduced, and he had a wide based ataxic gait. Initially diagnosis was uncertain and an encephalitis was considered possible. An EEG showed generalised slowing which was more prominent on the left and was consistent with cerebral vasculitis. Electromyography showed features of peripheral neuropathy. Brain CT and MRI were normal. Liver function tests were abnormal.

Alopecia and peripheral neuropathy raised the possibility of thallium poisoning. This was confirmed by toxin screening which disclosed high concentrations in blood (108 µg/l) and urine (1350 µg/l). Thallium is not normally present in the environment and no more than trace concentrations would be expected (<2 µg/l). Concentrations >100 µg/l in blood and 200 µg/l in urine are considered hazardous.²⁰

Psychiatric assessment during acute stages did not indicate abnormality of mood or suicidal intention. The poisoning was consid-

Department of Clinical Neuropsychology, Wolfson Rehabilitation Centre, London and Department of Psychology, University of Surrey, Guildford, UK
T M McMillan

Department of Neuropsychiatry, St George's Hospital, London, UK
R R Jacobson

Department of Neurology, Atkinson Morley's Hospital, London, UK
M Gross

Correspondence to: Professor T M McMillan, Department of Clinical, Neuropsychology, Wolfson Rehabilitation Centre and Atkinson Morley's Hospital, St George's Healthcare Trust, Copse Hill, Wimbledon London SW20 ONE.

Received 16 September 1996 and in revised form 26 March 1997
Accepted 8 April 1997

ered to be non-accidental, possibly via the water supply to the house, and the police were informed. Other members of the immediate family showed less severe symptoms of thallium poisoning, which did not require admission to hospital. He was treated with Prussian blue and potassium supplements.

He was discharged home in March and admitted a week later to the Wolfson Rehabilitation Centre for three months of neurorehabilitation.

He was seen four years after diagnosis for neurological follow up when urine thallium and MRI investigations showed no abnormality, but nerve conduction studies disclosed chronic peripheral neuropathy. His muscle power had partially improved and his gait was less widely based.

PERSONAL BACKGROUND

He had left school at the age of 16 without certificates and then worked in unskilled and semiskilled manual jobs for at least 10 years. He then worked as a computer operator for 10 years or more before obtaining work as a junior manager in a clerical and administrative capacity a year before the accident. His employer was interviewed by telephone and made no criticism of his performance at work before his illness.

He lived with a partner for 25 years in the upper floor of a two floor house. She was interviewed during the acute illness, rehabilitation, and at follow up with regard to his background and progress. The couple had two adult children (who were in their early 20s). He denied any prior psychiatric or neurological history. His personality before the poisoning would seem to have been somewhat obsessive, but without evidence of frank clinical abnormality and no known history of violence. He successfully pursued a claim for compensation in 1992 which was concluded in 1993.

MEDICATION

He was taking none at the time of any cognitive assessment.

NEUROPSYCHOLOGICAL ASSESSMENT (TABLE)

He was assessed three months after diagnosis during his admission for neurorehabilitation, again after discharge 12 months postdiagnosis, and once more four and a half years after diagnosis. He was compliant with testing.

GENERAL INTELLECT

His score on the national adult reading test (second edition) suggested that his verbal IQ was at worst, towards the upper margins of the high average range.²¹

Current intellect was assessed using the Wechsler adult intelligence scale-revised.²² Impairment of verbal IQ was suggested for the following reasons. Firstly, the 18 point discrepancy between verbal IQ and estimated premorbid verbal IQ using the national adult reading test (NART), is expected in less than 1% of the normal United Kingdom population.²¹ Secondly, the reliability of the discrepancy between verbal and performance IQ was signifi-

Table 1 Neuropsychology test results

	3 months	12 months	4.5 y*
National adult reading test (VIQ)	—	—	118
WAIS-R verbal IQ	—	—	100
WAIS-R performance IQ	—	—	114
Digit span (age scaled scores)	12	13	12
Vocabulary	8	9	10
Arithmetic	10	9	9
Comprehension	8	7	9
Similarities	7	10	11
Picture completion	—	—	12
Picture arrangement	—	—	11
Block design	12	15	16
Object assembly	10	13	15
Digit symbol	—	—	7
Information processing: (adjusted score)	49	50	51
Digit span (forward/back)	6/6	7/6	7/5
List learning	30	38	46
Prose recall (immediate)	6	16	7
Prose recall (delayed)	7	16	9
Rey-Osterrieth figure copy	33	35	35
Delayed recall	18	29	26
Trail making test A	42	60	50
Trail making test B	86	80	89
Verbal fluency (total)	28	32	30
Judgement of line orientation	27	30	29

* Time since 1st admission to district general hospital.

cant ($P < 0.05$) using Wechsler's United States norms,²² although this only raises a possibility of lateralised damage. This possibility is, however, of note because of the direction of the discrepancy (performance IQ > verbal IQ).²³ Thirdly, a laterality index of cognitive impairment, which was derived from principal components analysis of the WAIS-R population sample from the United States, was calculated,²⁴ and indicated a statistical likelihood of lateralised damage ($z = -2.11$, $P < 0.05$). Finally, abnormality of the verbal IQ-performance IQ score difference was considered. Scrutiny of subtest scores comprising the performance IQ scale showed a selective impairment on the digit symbol subtest which was significant ($P < 0.05$) using Crawford and Allan's United Kingdom norms.²⁵ This subtest requires motor speed, visual scanning, and learning. It is considered to be the subtest of the WAIS-R which is most sensitive to brain damage, but is not thought to be useful in determining localisation of injury.²⁶ In view of this, performance IQ was recalculated excluding the digit symbol subtest. The discrepancy between verbal IQ and performance IQ was then very abnormal (25 points) and statistically unusual compared with United Kingdom norms ($P < 0.05$).²⁵

INFORMATION PROCESSING²⁷

This test is visually presented. Two arrays of digits are shown, and a single digit which is not common to both arrays has to be cancelled with a pen. A time limit of four minutes is allowed for this test. The test score is adjusted to allow for motor speed, determined using a simple digit cancelling test, in which the subject simply has to cancel as many digits as possible within 20 seconds.²⁷ His adjusted score was below average for published age norms (63 (SD 19)), and was poorer than expected given his above average premorbid ability.

MEMORY

Forward and reverse digit span was average on all occasions. His ability to learn a 15 item word list over five trials²⁷ improved over successive testings, but remained below average for age norms (54.2 (SD 7.9)). Prose recall²⁵ was very poor on all given occasions (average 29 (SD 9)) without further decrement on recall after a delay. His copy of a complex geometric shape²⁸ was careless at the first assessment, and showed no abnormalities thereafter. Recall after a delay was initially average, and at later testing above average,²⁶ consistent with performance IQ.

EXECUTIVE FUNCTIONING

*Trail making test*²⁹

In part A, motor speed and visual scanning, are necessary. Time taken (seconds) was below average for his age (28 (SD 9)).²⁹ Part B requires flexibility of thinking in addition, and time taken (seconds) was also below average for his age (61 (SD 18))³⁰ and was poorer than expected. Verbal fluency on the three minute FAS test changed little over successive testing and remained well below average (49 (SD 6)).³¹ Impairment of colour vision was noted during his performance on the Stroop test. This was investigated by an ophthalmologist and is reported elsewhere.³²

VISUAL PERCEPTION

No evidence for impairment was found on Benton's judgement of line orientation test³³ in which his score approached or equalled the maximum of 30. Nor was there any sign of perceptual difficulties intercurrently on copy of the Rey figure or block design.

NEUROREHABILITATION

He was given an intensive programme of treatment for six weeks in March-April 1992. Therapists thought that this improved his function in terms of motor speed, stamina, gait, and balance. He was taught strategies to reduce the impact of his impaired memory and general slowness.

PSYCHIATRIC SEQUELAE

He was often irritable with aggressive outbursts. He impulsively and remorselessly assaulted members of his family and menaced people in the street. He lost his temper with a neighbour, whom he alleged had poisoned him. He had mild depressive but no general persecutory symptoms. His aggression responded well to 20 mg fluoxetine each morning.

Discussion

Only one other case has been published which reports neuropsychological effects of thallium poisoning in detail.¹³ In a case of accidental consumption, Thompson *et al*¹³ carried out neuropsychological testing seven months and 13 months after poisoning. The test scores were compared with those of a non-identical twin who had a similar career background and who had not been exposed. Both were of above average general intellect premorbidly. The poi-

soned twin had a selective impairment of non-verbal IQ (WAIS-R) at 13 months, estimated to be around 50 IQ points (from very superior to average). Thompson *et al*¹³ thought that this huge deficit could not be entirely explained by persisting perceptual-motor effects or by psychomotor slowness. Memory for new information was poor, especially for verbal material. The patient had a cardiac arrest in intensive care as a result of the poisoning, but was not thought to have had appreciable anoxia. An EEG showed signs of widespread abnormalities. Permanent cognitive impairment was thought to be a likely outcome.

Steinberg¹⁸ noted that there was impairment on psychological tests in three out of four cases, but gives very little detail. In one case persisting impairment on digit span and digit symbol subtests of the WAIS and on the Bender gestalt test was noted. Other published reports occasionally refer to impairment of concentration and memory and of general intellect after thallium poisoning but give no details.¹⁷

As in the case of Thompson *et al*,¹³ a lateralised effect was found here, but on this occasion impairment was found in verbal skills (verbal IQ, memory, and fluency) in this man, whose premorbid ability was above average but whose performance on these tests was below average. Consistent with impaired verbal skills was greater slowing of the EEG in the left hemisphere. It is of interest that very poor performance on the digit symbol test was found here by Thompson *et al*¹³ and is one of the few details noted by Steinberg.¹⁸ This test has been considered to be non-localising,²⁶ but relatively sensitive to brain injury caused by metals and other neurotoxins.³⁴

In the present case, persisting cognitive impairments were found with much lower initial blood and urine concentrations than reported by Thompson *et al*¹³ (serum 54 750 µg/l; urine 60 000 µg/l), although in their case, samples were probably taken within one to two days of consuming a single large dose rather than as here, after a few weeks of consumption of repeated lower doses.

On follow up four and a half years after injury, he had made a good physical recovery, was independently mobile, independent for self care, and was able to drive. Nevertheless there were serious persisting consequences for his daily life. He had returned to work about a year after the poisoning, but was made redundant after two months and was subsequently unsuccessful in obtaining further work. According to his own account and that of his partner, aggressive outbursts had impaired family and social functioning, until treatment with fluoxetine, after which he was no longer violent, but his temper remained a problem as did a preoccupation with the cause of the poisoning. He remained dependent on his partner for emotional support, this again being uncharacteristic of his preinjury personality. Given the length of time between injury and follow up these personality changes were considered permanent.

- 1 Mulkey J P, Oehme F W. A review of thallium toxicity. *Vet Hum Toxicol* 1993;35:445-53.
- 2 Allsop J L. Thallium poisoning. *Australian Annals of Medicine* 1953;2:144-60.
- 3 Prick J J G, Sillevs-Smitt W G, Muller L. *Thallium poisoning*. Amsterdam: Elsevier, 1955.
- 4 Bank W J, Pleasure D E, Suzukik, Nigro M, Katz R. Thallium poisoning. *Arch Neurol* 1972;26:456-64.
- 5 Villanueva E, Hernandez-Cueto C, Lachica E, Rodrigo M D, Ramos V. Poisoning by thallium: a study of five cases. *Drug Saf* 1990;5:384-9.
- 6 Cavanagh J B. What have we learnt from Graham Frederick Young? Reflections on the mechanism of thallium neurotoxicity. *Neuropathol Appl Neurobiol* 1991;17:3-9.
- 7 Ginsburg H M, Nixon C E. Thallium poisoning. *JAMA* 1932;98:1076-7.
- 8 Reed D, Crawley J, Faro S N, Pieper S J, Kurland L T. Thallotoxicosis. *JAMA* 1963;183:96-102.
- 9 Hamilton A, Hardy H L. *Industrial toxicology*. 3rd ed. Acton, MA: Publishing Sciences Group, 1976;175-6.
- 10 Bank W J. Thallium. In: P S Spencer, ed. *Clinical neurotoxicology*. Baltimore: William and Wilkins, 1980:570-7.
- 11 Bental E, Lavy S, Amir N. Electroencephalographic changes due to arsenic, thallium and strychnine poisoning. *Confinia Neurologica (Basel)* 1961;21:144-60.
- 12 Cavanagh J B, Fuller N H, Johnson H R M, Rudge P. The effects of thallium salts with particular reference to nervous system changes. *Q J Med* 1974;43:293-319.
- 13 Thompson C, Dent, J Saxby P. Effects of thallium poisoning on intellectual functioning. *Br J Psychiatry* 1988;155:396-9.
- 14 Kennedy P, Cavanagh J B. Spinal changes in the neuropathy of thallium poisoning. *J Neurol Sci* 1976;29:295-301.
- 15 Prick J J G. Thallium poisoning. In: P J Vinken, G W Van Bruyn, eds. *Handbook of chemical neurology*. New York: North Holland, 1979;36:239-78.
- 16 Inslay B M, Grufferman S, Ayliffe H E. Thallium poisoning in cocaine abusers. *Am J Emerg Med* 1980;4:545-8.
- 17 Vrij A A, Cremers H M H G, Lustermaans F A. Successful recovery of a patient with thallium poisoning. *Neth J Med* 1995;47:121-6.
- 18 Steinberg H J. Accidental thallium poisoning. *South Med J* 1961;54:6-9.
- 19 Moeschlin S. Thallium poisoning. *Clin Toxicol* 1980;17:133-46.
- 20 Wainwright A P, Kox W J, House I M, Henry J A, Heaton R, Seed W A. Clinical features and therapy of acute thallium poisoning. *QJM* 1988;69:939-44.
- 21 Nelson H E, Willison J. *National adult reading*. 2nd ed. Windsor: NFER Nelson, 1991.
- 22 Wechsler D. *Wechsler adult intelligence scale-revised*. New York: The Psychological Corporation, Harcourt Brace Jovanovich, 1981.
- 23 Crawford JR. Current and premorbid intelligence measures in neuropsychological assessment. In: JR Crawford, DM Parker, WW McKinlay, eds. *A handbook of neuropsychological assessment*. Hove: Lawrence Erlbaum, 1992:21-50.
- 24 Lawson JS, Inglis J, Stroud TWF. A laterality index of cognitive impairment derived from a principal components analysis of the WAIS-R. *J Consult Clin Psychol* 1983;51:841-7.
- 25 Crawford JR, Allan KM. WAIS-R sub-test scatter: base rate data from a healthy UK sample. *Br J Clin Psychol* 1996;35:235-47.
- 26 Lezak MD. *Neuropsychological assessment*. 3rd ed. New York: Oxford University Press, 1995.
- 27 Coughlan A K, Hollows S E. *The adult memory and information processing battery*. Leeds: St James' University Hospital, 1985.
- 28 Rey A. *L'examen clinique en psychologie*. Paris: Presses Universitaires de France, 1964.
- 29 Reitan R M. Validity of the trail making test as an indicator of organic brain damage. *Percept Mot Skills* 1958;8:271-6.
- 30 Stuss DT, Stethem LL, Pelchat G. Three tests of attention and rapid information processing: an extension. *The Clinical Neuropsychologist* 1988;2:246-50.
- 31 Benton A L, Hamsher K deS. *Multilingual aphasia examination*. Iowa City: Iowa AJA Associates, 1989.
- 32 Tabandeh H, Gowston, J G, Thompson G M. Ophthalmologic features of thallium poisoning. *Am J Ophthalmol* 1994;117:243-5.
- 33 Benton A L, Hamsher K deS, Varney H R, Spreen O. *Contributions to neuropsychological assessment*. New York: Oxford University Press, 1983.
- 34 Hartman D E. *Neuropsychological toxicology*. New York: Pergamon Press, 1988.