Fig (a) EEG recorded just before sodium valproate treatment showing generalised spike and wave discharges after 3 minutes of hyperventilation; intermittent photic stimulation at 15 Hz was ineffective. (b) EEG recorded 25 days following sodium valproate withdrawal showing no paroxysmal discharges at rest; intermittent photic stimulation at 20 Hz evoked generalised spike and wave discharges.

withdrawn at 13 years of age. Photic driving was occasionally seen during drug reduction. One month following sodium valproate withdrawal a generalised tonic-clonic convulsion occurred while she was playing a video game at home. EEG showed persistence of the left centro-temporal discharges and generalised spike and wave discharges evoked by intermittent photic stimulation. No further seizure or photoconvulsive response occurred afterwards, while off antiepileptic treatment.

That photosensitivity was temporally linked to sodium valproate withdrawal is beyond doubt. All patients had generalised convulsions under environmental flicker stimulation and photoconvulsive response a few weeks after sodium valproate reduction or withdrawal. Furthermore, photosensitivity rapidly disappeared off antiepileptic drugs in the third patient and on phenobarbitone in the second patient.² A causal relationship is also highly probable in the first two cases. Both patients showed photosensitivity at an age in which it does not usually develop.² Also, phenobarbitone withdrawal was not related to photosensitivity in the first case, at an age when photosensitivity may first appear. In spite of

age and type of epileptic syndrome, causal relationship between sodium valproate withdrawal and photosensitivity occurrence may be sustained even in the third case. In fact, tonic-clonic convulsions have been reported as a late relapse in benign partial epilepsy with rolandic spikes, not related to drug suspension;⁴ generalised spike and wave discharges are quite common on the EEG of affected children, but they are rarely evoked by intermittent photic stimulation;⁵ photosensitivity characteristically appears around puberty but persists for many years.⁶ Thus, it is unlikely that sodium valproate withdrawal triggered underlying previously developed photosensitivity. Finally, a family history of photosensitive epilepsy or of a photoconvulsive response without seizures, usually common in photosensitive epilepsy,⁷ is lacking in our patient.

The mechanism of occurrence of photosensitivity following sodium valproate withdrawal is unknown. Photosensitivity is usually rapidly controlled by sodium valproate. A rebound effect related to drug withdrawal may be supposed. Further cases are needed to establish whether this transient photosensitivity is really a consequence of drug withdrawal. In any case, epileptic

patients should avoid exposure to environmental flickering light during sodium valproate reduction and shortly after withdrawal.

GIOVANNI AMBROSETTI
CARLO ALBERTO TASSINARI
Istituto di Clinica Neurologica
Via Ugo Foscolo 7
40123 Bologna, Italy

References

- 1 Jeavons PM, Harding GFA. Photosensitive Epilepsy. *Clinics in Developmental Medicine* no. 56. London: Heinemann, 1975.
- 2 Newmark ME, Penry JK. Photosensitivity and Epilepsy: a Review. New York: Raven Press, 1979.
- 3 Bickford RG, Daly D, Keith HM. Convulsive effects of light stimulation in children. *Am J Dis Child* 1953;86:170-83.
- 4 Blom S, Heijbel J. Benign epilepsy of children with centro-temporal EEG foci: A follow-up study in adulthood of patients initially treated as children. *Epilepsia* 1982;23:629-32.
- 5 Aicardi J. *Epilepsy in Children*. New York: Raven Press, 1986, 122.
- 6 Jeavons PM, Bishop A, Harding GFA. The prognosis of photosensitivity. *Epilepsia* 1986;27:569-75.
- 7 Wilkins A, Lindsay J. Common forms of reflex epilepsy: Physiological mechanisms and techniques for treatment. In: Pedley PG, Moldrum BS, eds. *Recent Advances in Epilepsy*, Vol. 2. Edinburgh: Churchill Livingstone, 1985:239-71.

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Adult metachromatic leucodystrophy: an underdiagnosed disease?

Sir: Metachromatic leucodystrophy is an inherited autosomal recessive disease due to deficient activity of cerebroside sulphatase and is characterised by demyelination and accumulation of galactosyl-sulphatide in nervous and other tissues. It can begin at any time from infancy to late adult age,⁴ this probably depending on residual enzymatic activity.¹¹ Usually two fully distinct forms of the disease are recognised:¹³ late infantile and adult (juvenile cases overlap both, in clinical course, age at onset and duration of the disease).

The adult form is rare and peculiar in its psychiatric presentation, lack of family history and absence of neurological signs. Curiously it was the first to be recognised as such,^{2 10} but until a few years ago was rarely considered and diagnosed. Some authors

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had already suspected that the adult form was more common than generally believed. Recent progress in diagnostic techniques has confirmed this.

We report a case of a 33 year old woman who was admitted in September 1985 with a severe behavioural disorder that significantly altered her family and social relationships. No family history of mental and neurological illness was reported. Her parents were not consanguineous. The patient had a normal development, a PhD degree and worked as a journalist and literary translator. Her parents reported the beginning of her adult symptoms at age 27 years: she progressively neglected her family and personal affairs, manifested inappropriate affect, excessive sexual interest, mild reduction of recent memory and temporal disorientation; she never had hallucinations or convulsions. Two years later she was not able to maintain her employment. She started psychotherapy which lasted 3 years with no benefit; neuroleptic therapy also, after a new psychiatric referral, did not yield any improvement. The clinical situation progressively worsened leading the patient next to loose self control: mental deterioration, depression of mood, occasional urinary incontinence and the poor response to psychotropic therapy, suggested CT to her psychiatrist. This showed a diffuse alteration of white matter density with marked enlargement of ventricular system

and cortical sulci due to atrophy (fig).

On admission to our department the clinical picture of a severe dementing syndrome was prominent with apraxia, language impairment with frequent anomias, marked temporal disorientation, childish behaviour, loss of motor and verbal initiative, confabulation. Neurological examination revealed a slight increase of tone and tendon reflexes of left lower limb, general instability of posture and gait, which was wide based, a fine tremor of the outstretched fingers without weakness or atrophy. EEG showed a poorly organised rhythm 7-8 Hz, with irregular slow activity over the fronto-temporal regions. MRI confirmed the marked symmetrical alteration of the white matter and diffuse atrophy (fig). Patient's score with Raven Progressive Matrices was 4/36 (compared with mean value 24/36) showing a marked deterioration of cognitive functions and a typical frontal perseveration in answering. Since CSF analysis was normal and the EMG examination showed a polyneuropathic pattern with motor slowing of nerve conduction velocity (33.7 m/s and 37.4 m/s respectively for right and left common peroneal nerves), as an alternative to multiple sclerosis we considered adult leucodystrophic pathology. Arylsulphatase A level of patient's blood leucocytes was severely decreased (19 nM/hour/mg protein, with a normal range of 90-260), while the enzyme levels of her parents were indicative

of heterozygous state. The patient's younger sister, now aged 29 years, was perfectly healthy but she refused any medical investigation. Sural nerve biopsy showed accumulation of granules in the cytoplasm of Schwann cells and macrophages; these stained metachromatically with toluidine blue. Myelinated fibre population was reduced and many large diameter axons were surrounded by thinner than normal myelin sheaths. Ultrastructurally the accumulated material showed the configuration of lamellar zebra bodies and tuffstone bodies both of them considered to be suggestive of sulphatides.¹⁶

Our case raises the problem of psychiatric presentation of organic brain diseases,^{5,7} that often leads to misdiagnosis with long-lasting therapeutic and social implications for the patient and the family. In the context of a more "neutral" approach to such patients, an incomplete resolution of psychiatric symptoms, poor response to psychotherapy, any clue of selective neuropsychological impairment or sign of focal neurological damage, must lead the physician to check the diagnosis, with further appropriate investigations.

In our patient there was positive diagnostic information from EEG, nerve conduction study, nerve biopsy, enzymatic assay. The CSF was normal. Early alterations can be seen on CT examination.^{12,14} At our patient's disease stage CT conclusively changed the initial psychiatric diagnosis, while MRI did not yield additional information; MRI can be useful, however, to obtain early diagnosis.¹⁵ Neuropsychological assessment seems to be valuable in early evaluation of these patients: the pattern of selective spatial relationship deficit, contrasted with no impairment of verbal performance, has been suggested as indicative of organic brain damage.^{3,9}

We believe that metachromatic leucodystrophy with such an adult clinical onset is more frequent than generally considered. An investigation in an adult psychiatric population for biochemical abnormalities, provided surprising evidence of the presence of enzymatic defects in three of the 18 patients studied.⁸ No other similar investigation has since been carried out although in addition to the epidemiological, neurophysiological and therapeutic implications, such a study could lead to a better knowledge of the relationships among brain structure, function and symptoms. Early definition of the diagnosis is not only of theoretical interest: although the therapy of this metabolic disease is not satisfactory (bone marrow transplantation, if performed as soon as possible after birth, can only delay the neurological

Fig (a) CT scan shows dilated lateral ventricles, slightly widened cortical sulci and diffuse bilateral hypodensity of white matter. (b) axial magnetic resonance image of brain, passing through lateral ventricles. 0.5 T superconducting magnet, 10 mm section, spin-echo sequence: repetition time, 1050 ms; echo delay time, 50 ms. This sequence shows the marked, symmetrical increasing of white matter signal and the dilatation of ventricles and cortical sulci.

deterioration but not reverse the course of the disease), early genetic counselling is of great importance.

MASSIMO CERIZZA
RAFFAELLO NEMNI*

FILIPPO TAMMA

*The Neurological Clinic of Milan University,
S. Gerardo Hospital,
Monza, and
S. Raffaele Hospital,*
Segrate, Italy.*

Address for correspondence: Dr Massimo Cerizza, Clinica Neurologica, Ospedale S. Gerardo, Via Donizetti 106, 20052 Monza, Italy.

References

- Alves D, Pires MM, Guimarães A, Miranda MC. Four cases of late-onset metachromatic leukodystrophy in a family: clinical, biochemical and neuropathological studies. *J Neurol Neurosurg Psychiatry* 1986; **49**:1417-22.
- Austin J, Armstrong D, Fouch S, et al. Metachromatic Leukodystrophy (MLD). VIII. MLD in adults: diagnosis and pathogenesis. *Arch Neurol* 1968; **18**:225-40.
- Besson JAO. A diagnostic pointer to adult Metachromatic Leukodystrophy. *Br J Psychiatry* 1980; **137**:186-7.
- Bosch EP, Hart MN. Late adult-onset Metachromatic Leukodystrophy. Dementia and polyneuropathy in a 63-year-old man. *Arch Neurol* 1978; **35**:475-7.
- Cunningham Owens DG, Johnstone EC, Bydder GM, Kree L. Unsuspected organic disease in chronic schizophrenia demonstrated by computed tomography. *J Neurol Neurosurg Psychiatry* 1980; **43**:1065-9.
- Goebel HH, Argyrakakis A, Seidel D, et al. Adult metachromatic leukodystrophy. IV. Ultrastructural studies on the central and peripheral nervous system. *Eur Neurol* 1980; **19**:294-307.
- Hall RCW, Popkin RK, Devaul RA, et al. Physical illness presenting as psychiatric disease. *Arch Gen Psychiatry* 1978; **35**:1315-20.
- Mahon-Haft H, Stone RK, Johnson R, Shah S. Biochemical abnormalities of Metachromatic Leukodystrophy in an adult psychiatric population. *Am J Psychiatry* 1981; **138**:1372-4.
- Manowitz P, Kling A, Kohn H. Clinical course of adult metachromatic leukodystrophy presenting as schizophrenia. A report of two living cases in siblings. *J Nerv Ment Dis* 1978; **166**:500-6.
- Pilz H, Muller D. Studies on adult metachromatic leukodystrophy. II. Biochemical aspects of adult cases of MLD. *J Neurol Sci* 1969; **9**:585-95.
- Porter MT, Fluharty AL, Trammel J, et al. A correlation of intracellular cerebroside sulphatase activity in fibroblasts with latency in Metachromatic Leukodystrophy. *Biochem Biophys Res Commun* 1971; **44**:660-6.
- Schipper HI, Seidel D. Computed tomography in late-onset Metachromatic Leukodystrophy. *Neuroradiology* 1984; **26**:39-44.
- Seidel D, Heipertz R, Goebel HH, et al. Adult metachromatic leukodystrophy. III. Clinical course, final stages and first biochemical results. *Eur Neurol* 1980; **19**:288-93.
- Skomer C, Stears J, Austin J. Metachromatic Leukodystrophy (MLD). XV. Adult MLD with focal lesions by computed tomography. *Arch Neurol* 1983; **40**:354-5.
- Waltz G, Harik SI, Kaufman B. Adult metachromatic leukodystrophy. Value of computed tomographic scanning and magnetic resonance imaging of the brain. *Arch Neurol* 1987; **44**:225-7.

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Recovery from chronic solvent abuse

Sir: The evidence concerning impairment of cognitive functions in solvent abusers is still equivocal: reports have provided evidence both for¹⁻³ and against⁴⁻⁶ cognitive impairment. In studies reporting cognitive impairment the question of whether these effects are reversible has not been satisfactorily answered. Ron⁷ in a recent review article emphasised that one of the shortcomings of investigations into cognitive dysfunction as a result of solvent abuse is the lack of adequately controlled follow-up studies.

We had the opportunity to conduct a series of examinations on a chronic glue sniffer who had been detained in an institution for young offenders. The institutional setting ensured that he had no access to solvents after his remand and we were able to chart the time course of recovery of intel-

lectual functions over a period of 18 months under unusually controlled conditions.

Inmate AB (fictitious initials) who was 18 years old at the time of the initial interview came to our attention when he reported at the prison's medical centre complaining of drowsiness, sleeplessness, lack of concentration and memory disorders. He also suffered from poor co-ordination, unsteadiness of gait and general sluggishness. He stated that he had started inhaling solvents at the age of 13 years and continued until the day he was arrested for attempted rape which he had committed while under the influence of solvents. At the age of 16 he habitually consumed 250-500 ml of glue per day 3-4 days a week. Over the year before he was arrested, his consumption had increased to 500-750 ml per day. His experience with other drugs was restricted to isolated experiments with alcohol and cannabis. He almost exclusively used Evostik an adhesive which contains 48.5% toluene and 5.3% n-hexane (information obtained from the manufacturer).

On initial presentation AB had been in custody for 4 months: a time assumed to be well beyond the acute effects of intoxication and immediate withdrawal from solvents. He was assessed neuropsychologically on a variety of traditional measures and followed up at 3 monthly intervals using selected tests from a computerised test battery which covers a variety of functions including visual memory, attention, reaction time, visual search and word recognition. The computerised tests are repeatable, most without a significant training effect, and can be used to monitor recovery. AB was also assessed with

Table Summary of initial and follow-up results for AB and controls

	Initial assessment		18 months	12 months
	AB	Controls N = 12	AB	Controls N = 12
Visual memory span (blocks)	13.5	14.7 (3.5)	13.0	16.2 (3.5)
Event detection threshold (ms)	241†	31.1 (8.6)	22.5	32.6 (14.4)
Movement detection (no. errors: max = 25)	21†	5 (3.4)	6	3.8 (2.8)
Visual search (ms)	3772†	2692 (282)	2513	2294 (420)
Word recognition threshold (ms)	245†	60.2 (14.7)	110†	56 (13.8)
Body sway (deg/min)	17.7†	4.9 (1.6)	4.6	3.5 (1.6)
Reaction time: simple (msecs)				
Decision time	319*	254 (30.3)	305	260 (30.7)
Movement time	297†	195 (20.7)	237*	157 (29.6)
Choice (ms)				
Decision time	344	295 (27.8)	308	194 (26.9)
Movement time	341†	198 (24.3)	217*	159 (28.5)

Figures in brackets are standard deviations.

*Differences > two SDs. †Differences > three SDs.