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Occupational lead neurotoxicity: a behavioural and electrophysiological evaluation

Study design and year one results

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ABSTRACT To evaluate the effects of chronic lead exposure on the nervous system in adults, a set of neurobehavioural and electrophysiological tests was administered to 99 lead exposed foundry employees and 61 unexposed workers. Current and past blood lead concentrations were used to estimate the degree of lead absorption; all previous blood lead concentrations had been less than or equal to 90 μg/100 ml. Characteristic signs (such as wrist extensor weakness) or symptoms (such as colic) of lead poisoning were not seen. Sensory conduction in the sural nerve was modestly slowed by lead exposure but conduction in the ulnar and peroneal nerves was not affected. By contrast, various neurobehavioural functions deteriorated with increasing lead burden. Workers with blood lead concentrations between 40 and 60 μg/100 ml showed impaired performance on tests of verbal concept formation, visual/motor performance, memory, and mood. Thus impairment in central nervous system function in lead exposed adults occurred in the absence of peripheral nervous system derangement and increased in severity with increasing lead dose.

Although the earliest effect of systemic lead absorption is the inhibition of various enzyme systems, particularly those regulating haem synthesis[1] and mitochondrial respiration,[2] organ dysfunction, sufficient to cause symptoms, usually first occurs in the nervous system. In the past[3] lead poisoning was often associated with signs of toxic encephalopathy and overt peripheral neuropathy. As levels of exposure have fallen, lead neurotoxicity has been manifested by more subtle disturbances of affect, psychomotor function, and nerve conduction.[4]

Epidemiological investigations have not consistently characterised these disorders, some have shown slowing of motor nerve conduction,[5-8] others have not.[9 10] Impaired psychomotor function has been reported by most groups[11-14] but the degree of impairment found has varied. These inconsistencies may be attributed, in part, to limitations in study design and inadequate standardisation of techniques. All previous studies, except that of Spivey and colleagues,[9 10] have been cross sectional investigations comparing a group of lead exposed workers with an unexposed referent population. In such studies the course of exposure related disorders is not directly evaluated.[15] Despite statements in most papers that "standard techniques were used," the degree to which technical factors (stimulus intensity and limb temperature in nerve conduction testing, for example) were controlled is unclear. More importantly, many fail adequately to control for potential confounding factors such as age and education level in neurobehavioural measures.

Currently, nerve conduction velocity measurement is viewed as an early indicator of lead induced nervous system damage[5] and, as such, is used widely in the clinical assessment of lead exposed workers. Despite the demonstration of adverse effects on behavioural function in lead workers with modest levels of absorption (blood lead concentrations be-

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tween 40 and 60 μg/dl)[14] neurobehavioural testing is not used as frequently in the evaluation of patients. In the report of Repko *et al* both neurobehavioural and neurophysiological techniques were used, but the relative value of these tests in the early detection of lead toxicity was not directly evaluated.[11]

In the present report we describe an investigation of lead exposed workers designed to evaluate the effects of chronic low level lead exposure on the nervous system. By applying a comprehensive set of neurobehavioural and neurophysiological tests to groups with varying degrees of lead absorption, we are able to explore dose response relationships in workers with chronic exposure to lead. By using both types of testing in the study, we are also able to identify the techniques most sensitive to the manifestations of subclinical lead neurotoxicity. The present paper describes the first year of a three year project.

Methods

SUBJECTS

Between May 1980 and June 1981, 106 lead exposed foundry workers were tested. They constituted 91% of the current lead exposed production workers at the foundry: the remaining 9% either refused to participate in our study or were absent from work during the period of testing. Workers already employed in May 1980 were tested then, those hired during the following 13 months were tested soon after beginning work.

Sixty five workers in an assembly plant located adjacent to the foundry were also tested. Detailed job histories were obtained and a walk through plant survey was performed to ensure that the assembly workers were not exposed to lead or other neurotoxins. They were recruited from four work areas, employing 110 individuals, whose job duties and pay rates closely resembled those of the lead exposed workers. The unexposed workers resided in the same area as the exposed workers and most had attended the same schools. All tested workers were white and spoke English as their first language. None had blood lead concentrations over 90 μg/dl since beginning work at the plant, and none had been diagnosed as having lead poisoning.

Workers who drank heavily or had a history of severe head injury were not tested. Eleven individuals (seven exposed and four referents) were tested but were subsequently excluded from the data analysis because of insufficient data or because they had histories of acute alcohol use, previous alcoholism, psychoactive drug use, prior lead or solvent exposure, diabetes, or meningitis. Subsequent analyses therefore, relate to the residual 99 exposed and 61 referent workers studied. We also deleted data on certain tests from an individual's file if we thought that a confounding factor would affect performance on those tests but not on others using exclusion criteria which were developed a priori. Individuals were evaluated for exclusion without knowledge of test outcome or exposure. Individual results for the 14 with right arm or hand injury were deleted from analyses of tests of ulnar nerve conduction and the Santa Ana test using the right hand. The 13 with left arm or hand injury were removed from analyses of data on the Santa Ana test (left hand). We removed data on two individuals with foot or leg injuries from sural and peroneal nerve conduction analyses, two with epilepsy from all neurobehavioural tests, and one with frostbite and one with knee surgery from sural and peroneal nerve conduction analyses. Separate analyses showed that the test scores of these excluded individuals differed little from those not excluded. Nevertheless, in view of the prospective nature of this study, we thought it advisable to remove them from these and subsequent analyses to reduce potential confounding effects. All participants were informed of the risks and benefits of participation in the study and all medical data were treated confidentially. The employer had access only to data required by law under existing standards of the Occupational Safety and Health Administration.

EVALUATIVE PROCEDURES

Each individual received a questionnaire, a neurological examination, neurobehavioural testing, and blood and urine analyses. Most workers also underwent nerve conduction testing, although this was not performed at four testing sessions due to the unavailability of the testers and equipment. One individual refused to undergo nerve conduction testing but participated in other phases of the evaluation. Testing was performed during normal working hours in plant premises. In some instances, production constraints required that workers return to their jobs before finishing the entire testing sequence resulting in incomplete data files for a few individuals.

The questionnaire included detailed occupational, medical, hobby and social histories, including specific questions on alcohol intake and educational background. A physician performed the neurological examination.

Nerve conduction testing[16] was performed in a warm room using a Teca 4 electromyograph, equipped with differential amplifiers and an electronic averager. Each response was recorded using a fibreoptic graphic recorder, and response amplitudes and latencies were measured directly from the permanent record. Distances were measured with a tape measure. The skin temperature of each extremity was measured during testing using surface electrodes attached to a digital reading thermostat and was maintained at 33-36°C during testing by warming or cooling as needed. Motor responses were obtained using supramaximal stimulation. Sensory responses were elicited using 32 repetitive stimuli with responses averaged electronically and recorded. The recording electrode position was varied to ensure that sensory responses were recorded directly over the nerve being studied. The right arm and leg were studied in all individuals.

Neurobehavioural testing procedures described in greater detail previously[17] included subtests of the Wechsler Memory Scale (WMS),[18] the Wechsler Adult Intelligence Scale (WAIS),[19] the Continuous Performance Test,[20] the Santa Ana Dexterity Test,[21] and the Profile of Mood States (POMS).[22] Testing was performed by, or under the direction of, a clinical neuropsychologist using the procedures specified in the administration manual for each test. To reduce administration time, alternate items of the vocabulary subtest of the WAIS were used.

Whole blood lead concentrations were determined by anodic stripping voltammetry[23] on venous blood samples obtained by venepuncture in lead free vacuum tubes. Blood lead analyses before October 1980 were performed by a certified state laboratory. The commercial laboratory (Environmental Science Associates, Bedford, MA) which performed our analyses subsequently is also certified by the Center for Disease Control (CDC) for lead analysis and has been used as a reference laboratory by the CDC. This laboratory performs all analyses in duplicate and accepts only those results that agree within 5%. Blood zinc protoporphyrin determinations were performed but analytical errors were discovered which forced us to discard the results. Exhaled breath carbon monoxide levels were measured before and after behavioural testing using the Ecolyzer (Energetics Science Co).

To assess the comparability of blood lead concentrations obtained from the two laboratories, 28 blood samples obtained from another population were split between the two laboratories and a linear regression equation was derived to relate the results from the two laboratories. The results ranged from 12 to 96 μg/100 ml and agreed well ($r = 0{\cdot}92$). The equation relating the two laboratories was:

$$\text{Commercial lab value} = 6{\cdot}97 + (0{\cdot}961 \times \text{state lab value})$$

This equation was used to adjust the state values to those of the commercial laboratory.

STATISTICAL ANALYSES

Exposure characterisation – Using blood test results and employment histories, we calculated the time weighted average blood lead concentration over the 12 month period before our testing (TWA-12 months) as a summary of cumulative past exposure for foundry workers only. The blood lead concentration measured on the day of testing was used to indicate current exposure. Blood lead concentrations of exposed workers during the months before being hired were assumed to equal the mean level for unexposed workers.

Control of confounding – To adjust for the effects of age, sex, and education on neurobehavioural tests, and the effects of age, height, weight, and limb temperature on nerve conduction measurements, multiple linear regression analysis[24] of the data obtained from the unexposed population was used to develop a prediction equation for each test. Predicted values were derived for each individual using these equations, and the ratio of actual to predicted was computed (and multiplied by 100) to give a percent predicted value for each individual's performance on each test. A more detailed explanation of this process as it relates to our neurobehavioural tests appears elsewhere.[17]

Evaluation of dose response relationships – To assess the relationship of current blood lead concentration to test performance, individuals were grouped into four exposure categories, according to blood lead concentration on the day of testing, and the group means of the percent predicted values for each test were calculated. An exposure group whose performance was comparable to the referent population on a particular test should have an average percent predicted score near 100. In most tests, if lead exposure impairs performance, test scores for those in the higher exposure groups average below 100%. The opposite relationship holds for five of the POMS subtests (all except the Vigor scale): in this case large raw scores indicate an adverse effect and, therefore, percent predicted scores increase with excess reporting of symptoms. To evaluate the cumulative effect of lead exposure, the TWA-12 months exposure measure and appropriate confounding variables were included in a multiple regression analysis. The one sided significance level (p value) of the exposure term was calculated using the t statistic.[24] One sided testing was thought to be justified since no previous study has shown lead exposure to have a beneficial effect on neurological function.

Results

GROUP CHARACTERISTICS

Blood lead concentrations of the "unexposed"

Table 1 *Characteristics of population (n = 160)*

Age	Mean (range)	32·4 (18–62)
Company duration (months)	Mean (range)	33·6 (0–252)
Job duration (months)	Mean (range)	23·4 (0–252)
Years of schooling	Mean (range)	10·9 (5–16)
No of men (%)		129 (80·6)
Alcohol consumption:		
Non-drinker		17 (10·6)
Drink less than once a week		40 (25·0)
Drink once a week to less than once a day		69 (43·1)
Drink once or more a day		33 (20·6)
Not known		1 (0·6)
Blood lead concentration (μg/ml)	Mean (range)	32·8 (10–80)

workers ranged from 10 to 42 μg/100 ml, while the exposed ranged from 13 to 80 μg/100 ml. In view of this overlap between the two groups we combined the groups and stratified them in subsequent analyses based on measured blood lead concentrations. As a result, the two lowest exposure strata (current blood lead concentration: 0–20 μg/100 ml and 21–40 μg/100 ml) contain individuals from both the foundry and the assembly plant. Table 1 shows the characteristics of the composite population.

SYMPTOM RATES

We did not observe increased reporting of abdominal colic or other gastrointestinal symptoms typically associated with overt plumbism (table 2). In fact, the only symptom reported in excess was excessive tiredness, and this was noted only by individuals with blood lead concentrations above 60 μg/dl. The relative paucity of workers with blood lead concentrations above 60 μg/dl restricts the usefulness of data from this group for these and subsequent analyses. Individuals with blood concentrations between 40 and 60 μg/dl did not report symptoms to a greater extent than those with lower blood concentrations.

Table 2 *Symptom prevalence rates by blood lead concentration on the day of testing*

	Current blood lead concentration (μg/dl)			
Symptom	*0–20 (n = 26)*	*21–40 (n = 97)*	*41–60 (n = 28)*	*61–80 (n = 9)*
Joint pain	7·7%	11·6%	11·1%	11·1%
Numb arms	19·2	11·6	10·7	33·3
Numb legs	15·4	4·2	0	0
Weak arms	0	3·2	7·1	0
Weak legs	0	4·2	3·6	0
Incoordination	3·9	2·1	3·6	11·1
Headache	4·4	2·2	0	22·2
Irritability	17·4	4·3	7·1	11·1
Increased sleeping	8·7	5·4	10·7	11·1
Excessive tiredness	23·1	10·5	14·3	66·7
Confusion	0	2·1	0	22·2
Trouble remembering	11·5	9·5	10·7	33·3
Abdominal cramps	0	2·1	0	11·1
Nausea	3·9	1·1	0	11·1
Vomiting	7·7	0	3·6	0

Table 3 *Nerve conduction testing by blood lead concentration on day of testing, mean (SE)*

	Current blood lead concentration (μg/dl)			
	0–20 (n = 20)	*21–40 (n = 75)*	*41–60 (n = 17)*	*61–80 (n = 5)*
Ulnar nerve				
Motor conduction:				
Velocity (forearm) (m/s)	62·48 (1·75)	63·54 (0·92)	64·57 (2·58)	63·44 (1·43)
Amplitude (stimulation at wrist) (mv)	10·26 (0·48)	10·07 (0·27)	8·76 (0·56)	8·40 (0·78)
Amplitude (stimulation at elbow) (mv)	9·65 (0·50)	9·20 (0·26)	7·82 (0·45)	7·30 (0·77)
Distal latency (wrist time)	2·55 (0·10)	2·59 (0·04)	2·69 (0·12)	2·28 (0·12)
Sensory conduction:				
Velocity (m/s)	51·76 (1·50)	53·40 (0·74)	53·32 (1·81)	55·13 (1·56)
Amplitude (mv)	15·61 (1·48)	13·28 (0·74)	13·27 (1·37)	13·00 (1·53)
Peroneal nerve				
Motor conduction:				
Velocity (m/s)	50·82 (1·35)	49·92 (0·59)	49·88 (1·90)	52·61 (2·32)
Amplitude (stimulation at ankle) (mv)	5·15 (0·53)	5·20 (0·27)	5·53 (0·33)	7·10 (1·62)
Amplitude (stimulation at fibular head) (mv)	4·48 (0·50)	4·65 (0·25)	4·70 (0·39)	7·00 (1·41)
Distal latency (time)	4·42 (0·29)	4·27 (0·09)	4·21 (0·16)	3·66 (0·16)
Sural nerve				
Sensory conduction:				
Velocity (m/s)	48·70 (1·20)	47·84 (0·51)	46·29 (0·88)	45·40 (2·91)
Amplitude (mv)	16·42 (1·70)	14·32 (0·84)	14·10 (1·26)	11·40 (2·52)

Table 4 *Regression analysis of exposure indices versus nerve conduction parameters*

Nerve conduction parameter	*Significance level for exposure coefficient**	
	Current blood lead level	*Average exposure for previous 12 months*
Ulnar nerve		
Motor conduction (n = 65):		
Velocity (forearm)	0·50	0·21
Amplitude (wrist stimulation)	0·03	0·02
Amplitude (elbow stimulation)	0·003	0·004
Distal latency (wrist time)	0·47	0·70
Sensory conduction (n = 58):		
Velocity	0·10	0·02
Amplitude	0·16	0·06
Peroneal nerve		
Motor conduction (n = 60):		
Velocity	0·70	0·36
Amplitude (ankle stimulation)	0·35	0·36
Amplitude (fibular head stimulation)	0·64	0·55
Distal latency (time)	0·16	0·09
Sural nerve		
Sensory conduction (n = 60):		
Velocity	0·02	0·03
Amplitude	0·01	0·01

*Each tabulated value is significance level (p-value) associated with coefficient of an exposure index in a multiple linear regression model. The p-value corresponds to a one sided t test of the hypothesis that exposure has no effect on nerve conduction—that is, the exposure coefficient is zero. The regression model also incorporates terms that adjust for age, height, and weight (and limb temperature for the velocity parameters).

Table 5 *Neurobehavioural testing by blood lead concentration on day of testing, mean (SE)*

	Current blood lead concentration (μg/dl)			
	0–20 (n = 26)	*21–40 (n = 97)*	*41–60 (n = 28)*	*61–80 (n = 9)*
Wechsler Adult Intelligence Scale:				
Vocabulary	36·15 (3·49)	38·99 (1·49)	35·96 (3·33)	30·00 (4·89)
Similarities	13·11 (1·26)	14·40 (0·47)	11·19 (0·95)	12·44 (1·23)
Block design	32·19 (1·60)	33·96 (0·84)	31·16 (1·59)	35·33 (2·37)
Digit symbol	49·00 (2·01)	53·54 (1·30)	48·50 (2·46)	50·56 (3·21)
Digit symbol: recall	6·54 (0·43)	6·62 (0·25)	5·83 (0·46)	6·33 (0·99)
Wechsler Memory Scale:				
Information	5·29 (0·17)	5·36 (0·11)	4·55 (0·25)	5·33 (0·24)
Orientation	4·94 (0·06)	4·91 (0·03)	4·73 (0·12)	4·67 (0·17)
Mental control	6·82 (0·38)	7·08 (0·18)	6·68 (0·42)	5·67 (0·96)
Logical memory B	5·65 (0·68)	6·81 (0·46)	5·64 (0·87)	6·33 (1·25))
Digit span: forward	6·59 (0·21)	6·38 (0·13)	6·64 (0·19)	6·00 (0·37)
Digit span: backward	4·35 (0·24)	4·56 (0·12)	3·88 (0·30)	4·00 (0·29)
Visual reproduction	9·88 (0·70)	10·07 (0·30)	8·14 (0·70)	8·67 (1·14)
Paired associate learning	13·32 (1·79)	16·02 (0·96)	11·58 (1·47)	11·44 (2·91)
Continuous Performance:				
Mean response latency (msec)	485·0 (23·4)	447·9 (10·8)	462·4 (16·3)	524·5 (35·1)
Profile of mood states:				
Tension	10·73 (1·46)	10·49 (0·59)	9·60 (0·99)	15·11 (1·80)
Anger	7·85 (1·21)	7·81 (0·78)	9·20 (1·29)	12·89 (2·49)
Depression	7·27 (1·46)	8·03 (0·94)	7·68 (1·46)	12·78 (3·51)
Vigour	17·46 (1·13)	18·57 (0·59)	17·60 (1·28)	14·00 (1·55)
Fatigue	7·35 (1·38)	6·28 (0·49)	7·80 (1·11)	10·33 (2·24)
Confusion	6·81 (0·82)	5·88 (0·44)	6·08 (0·62)	10·33 (1·89)
Santa Ana:				
Preferred	22·52 (0·83)	24·64 (0·35)	23·14 (0·62)	24·72 (0·88)
Non-preferred	23·31 (0·83)	23·66 (0·38)	22·17 (0·67)	23·11 (1·11)
Both	29·55 (1·49)	31·41 (0·79)	29·80 (1·27)	29·00 (1·18)

NERVE CONDUCTION TESTING

Motor conduction in the ulnar and peroneal nerves did not deteriorate with increasing blood lead concentration except for reductions in the amplitude of the evoked motor potentials in the ulnar nerve (table 3). Modest slowing of sensory conduction and reduction of response amplitude were seen in the sural nerve. Regression analysis (table 4), using either current or cumulative (TWA 12 months) exposure indices, confirms these associations. In most instances current and cumulative exposure indices correlated equally well with effect parameters.

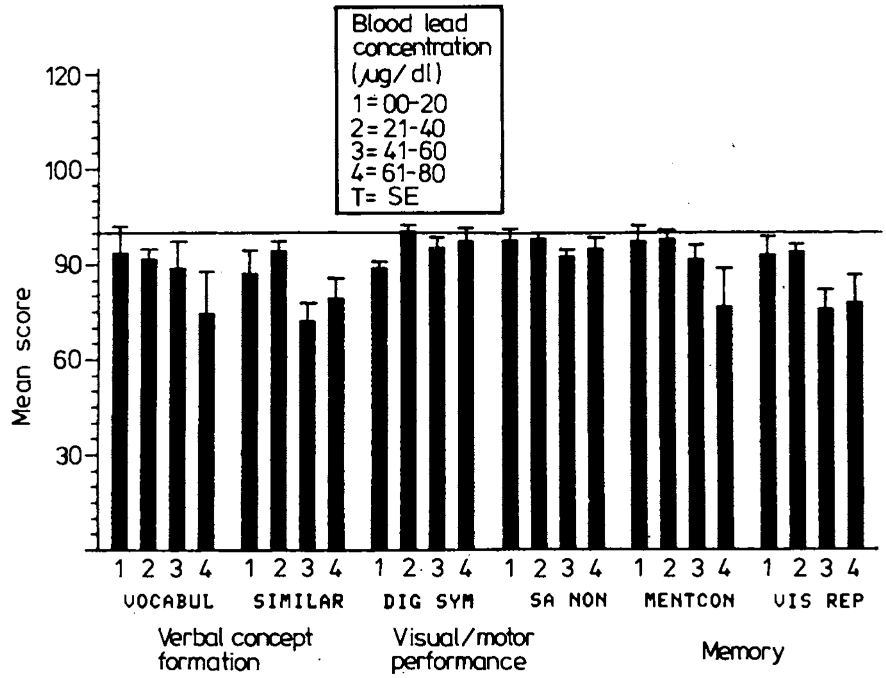

Fig 1 *Mean percent predicted scores on selected neurobehavioural tests by level of lead exposure.*

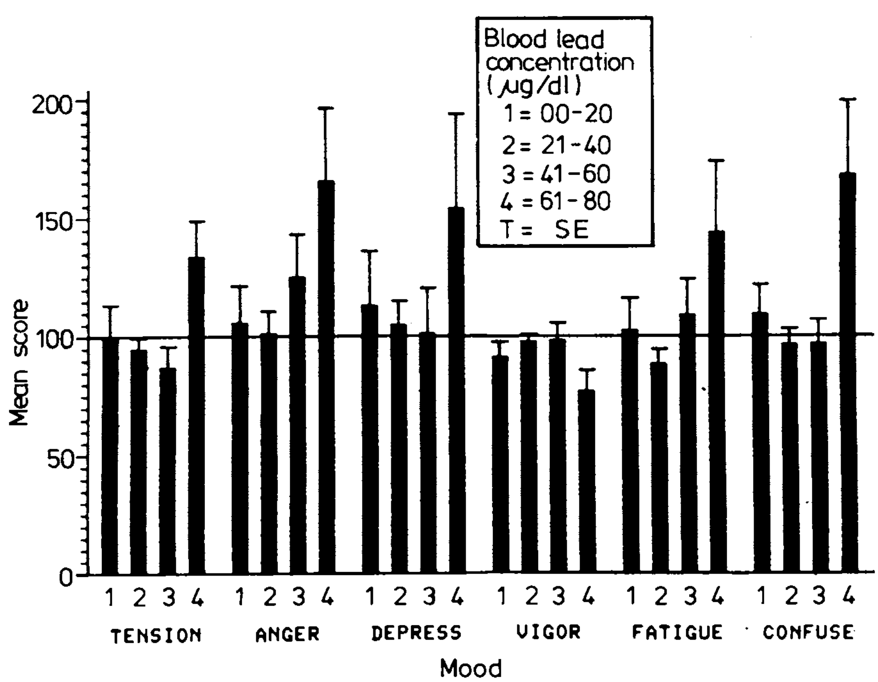

Fig 2 *Mean percent predicted scores on the profile of mood states (POMS) by level of lead exposure.*

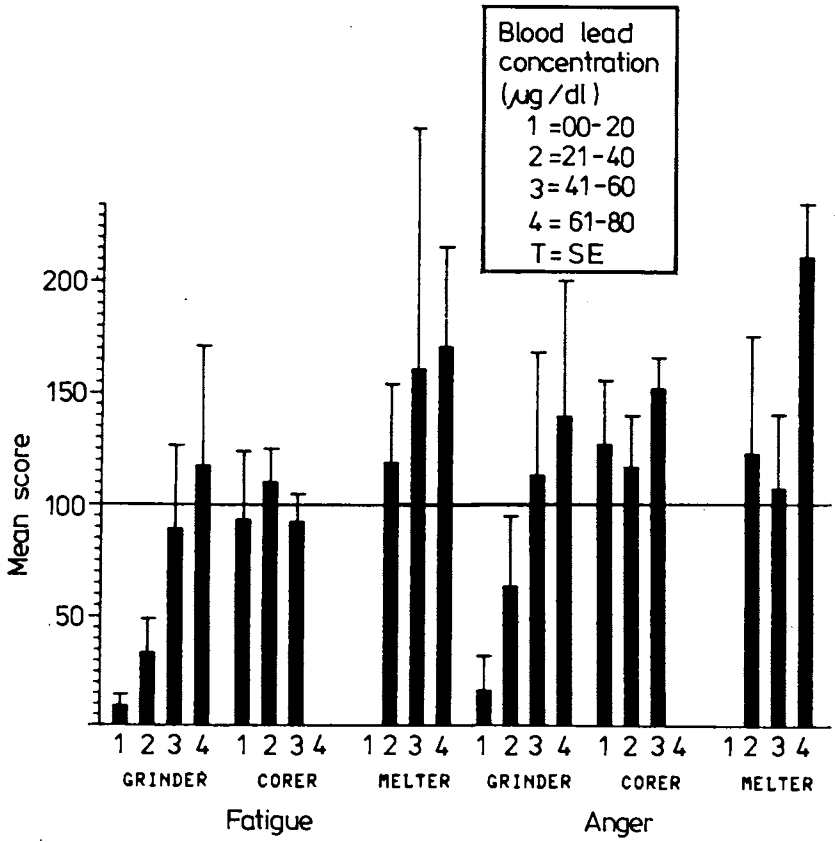

Fig 3 *Depression scores for categories of lead exposed workers.*

NEUROBEHAVIOURAL TESTING

Impairment in neurobehavioural function was particularly apparent in performance on tests of verbal concept formation, selected memory tests, and mood profile for individuals with blood lead concentrations above 40 µg/dl when comparing either mean raw scores (table 5) or adjusted scores (figs 1 and 2). Those with blood levels over 60 µg/dl showed even greater degrees of dysfunction. Tests that were sensitive to the effects of lead included the vocabulary and similarities subtests of the WAIS; the digit span (backwards), paired associate learning, mental control, and visual reproduction subtests of the WMS; and most of the POMS subtests.

Since some of the behavioural functions could have been influenced by job stress and aspects of the work experience which were correlated with lead exposure level, confounding by job characteristics was evaluated. Since subjective reports of mood are particularly sensitive to such job specific influences, we analysed scores on the POMS test within individual job category using the three largest job groups in the foundry, 12 melter pourers, 41 core makers, and 19 grinders. These jobs have different demands and levels of apparent health risk. Increasing reports of anger and fatigue were seen as blood lead concentrations increased for all job categories (fig 3).

Multiple regression analysis (table 6) showed that exposure level was significantly correlated ($p < 0.05$) with performance on tests of visual intelligence, memory, and various subtests of the POMS. A borderline association ($p = 0.06$) was seen between cumulative exposure and response latency on the continuous performance test. Current exposure level correlated with neurobehavioural test performance somewhat better than did cumulative exposure.

Table 6 *Regression analysis of exposure indices versus neurobehavioural tests*

	*Significance level for exposure coefficient**	
	Current blood lead concentration	*Average exposure for previous 12 months*
Wechsler Adult Intelligence Scale (n = 151):		
Vocabulary	0·04	0·08
Similarities	0·04	0·19
Block design	0·51	0·41
Digit symbol	0·74	0·92
Digit symbol: recall	0·37	0·79
Paired associate learning	0·12	0·77
Wechsler Memory Scale (n = 124):		
Information	0·32	0·68
Orientation	0·42	0·36
Mental control	0·02	0·16
Logical memory	0·78	0·75
Digit span: forward	0·54	0·50
Digit span: backward	0·09	0·24
Visual reproduction	0·23	0·65
Other tests:		
Continuous performance (n = 130) (mean response latency)	0·16	0·06
Profile of mood states (n = 153)		
Tension	0·07	0·06
Anger	0·01	0·01
Depression	0·04	0·02
Vigour	0·55	0·65
Fatigue	0·05	0·002
Confusion	0·01	0·04
Santa Ana dexterity (n = 134)		
Preferred hand	0·21	0·43
Non-preferred hand	0·15	0·26
Both hands	0·51	0·58

*Each tabulated value is the significance level (p value) associated with the coefficient of an exposure index in a multiple linear regression model. The p value corresponds to a one sided t test of the hypothesis that exposure has no effect on test performance — that is, the exposure coefficient is zero. Regression model also incorporates terms that adjust for age, gender, and education.

Discussion

These data support the view that lead exposure in adults causes dose dependent impairment of neurobehavioural function. Lead toxicity in these workers was manifested primarily as a disturbance in mood (leading to increased reports of depression, fatigue, tension, anger, and confusion). Short term memory (partially visual memory), psychomotor speed and dexterity, and verbal concept formation were also affected. Nerve conduction abnormalities were limited primarily to mild disruption in sensory conduction of the ulnar and sural nerves. These signs of toxicity occurred in individuals who did not report the classic symptoms of lead poisoning (colic, constipation, or wrist weakness for example) and whose blood lead concentrations were relatively low (below 80 μg/dl) and had never exceeded 90 μg/dl.

We have controlled for confounding as an explanation for these results by developing multivariate prediction equations based on a referent population[17] which allowed us to control for age, sex, and education effects on neurobehavioural tests and age, height, weight, and limb temperature in nerve conduction testing. As a result, confounding by these determinants of test outcome was minimised. We also investigated potential confounding effects of alcohol consumption, and carbon monoxide exposure, although these factors may have influenced test performance in some cases, they were not correlated with lead exposure level and, as such, would not distort the results.[25] Information bias was not likely since testers and testees were not aware of the blood lead concentration of individuals being tested. Within job groups, where perception of level of lead exposure would have been comparable among workers sharing the same job duties (fig 3), dose related changes in central nervous system symptomatology were seen.

Our data confirm and extend prior reports of impaired neurobehavioural performance in workers exposed to lead. We saw limited evidence of lead related impairment of psychomotor speed and dexterity, which has been reported by others in adults[7-10] and children.[26] We did observe effects of lead on short term memory and verbal intelligence. Our observation of mood changes in lead workers has not been related to blood lead concentrations in the manner reported here, although previous descriptions of lead toxicity[27 28] have noted increased central nervous system symptomatology.

The dose response assessment performed in this study suggests significant adverse neurobehavioural effects on adults with blood lead concentrations of

40–60 μg/dl. Although prior work by Hänninen *et al* indicates psychomotor slowing and impaired visual intelligence in workers with blood lead concentrations in this range,[14] effects on memory, verbal intelligence, and mood have not been clearly shown at this level of exposure. The reports of Valciukas *et al*[12] and Grandjean *et al*[13] include individuals with blood lead concentrations above 60 μg/dl and do not present stratified analyses of data which would permit comparison with the current form of analysis. Qualitatively, the types of neurobehavioural abnormality that we noted are similar to those noted at higher exposure levels in these reports. Increased rates of subjective symptoms of fatigue, forgetfulness, and restlessness were reported by Repko,[11] Baker *et al*,[27] and Lilis *et al*[28] in individuals with blood lead concentrations below 80 μg/dl.

We did not observe impaired nerve conduction velocities in motor nerves as previously noted by Seppäläinen and Hernberg,[5] Araki and Honma,[6] Buchthal and Behse,[7] and Feldman *et al*.[8] Since exposure levels were somewhat lower among our group than in some studies, a failure to find an association may reflect different dose levels. We did note modest loss of amplitude in the ulnar and sural nerves which has been observed by others and may correlate with subtle histological axonal changes previously noted in lead exposed workers.[7]

From these observations, it appears that initial signs of lead toxicity in adults become manifest in the central nervous system (CNS) as abnormalities of memory, psychomotor functions, and abstract concept formation well before overt disruption of the peripheral nervous system (PNS) occurs. Predominance of CNS effects after lead exposure may be attributable to selective vulnerability of the central nervous system resulting in a different dose response relationship between the central and peripheral nervous systems. Dysfunction of the PNS manifesting as slowed nerve conduction appears to require moderately raised blood lead concentrations (usually exceeding 60 μg/dl) for an extended period (usually more than six months). Central nervous system effects seem to occur at somewhat lower blood lead concentrations and may occur sooner. Our findings contrast directly with the previous view that lead neurotoxicity affects primarily the peripheral nervous system in adults and the central nervous system in children. CNS effects do appear early in the course of adult lead toxicity.

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