Cognitive functioning in lead workers

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ABSTRACT In a cross sectional study of occupational exposure to inorganic lead 91 men performed a series of microcomputer based tasks assessing sensor motor reaction time, memory, attention, verbal reasoning, and spatial processing. Performance on the tasks was studied in relation to three ranges of blood lead concentration (low, < 20 µg/dl; medium, 21–40 µg/dl; and high, 41–80 µg/dl) and exposure-response correlations for blood lead concentration, zinc protoporphyrin (Z PP) (range 7–210 µg/dl), and urinary aminolaevulinic acid (ALA) (range 0.5–22.0 mg/l). The results show that the high group were impaired on most of the tasks used and, in general, the magnitude of the impairment correlated better with blood lead concentration than Z PP or urinary ALA. An examination of the patterns of task impairment indicated a general slowing of sensory motor reaction time which was relatively independent of the nature of the cognitive functions being tested. There was some evidence, however, suggesting mild impairment of attention, verbal memory, and linguistic processing. In general, workers with high blood lead concentrations showed clear impairment of sensory motor functions in the absence of correspondingly strong evidence for impaired processing and memory functions. It is argued that a general slowness in responding may underlie many previous reports of widespread cognitive impairment in lead workers.

Evidence now accumulating indicates that occupational exposure to inorganic lead may impair central nervous system function¹ but, in contrast to our understanding of the effects of lead on biological systems,² it remains unclear which psychological functions are adversely affected. Much of this uncertainty derives from the heterogeneous and unsystematic exploration of psychological functions previously undertaken and this is often compounded by restricted analysis of task performance based on a single score.³

A review of the neurobehavioural publications on occupational exposure to lead shows that test batteries have usually comprised a selection of items from standard intelligence tests, together with tasks of sensory motor speed and coordination.^{1,4,5} Whereas intelligence test items are well standardised, they are not particularly suitable for exploring cognitive functions because performance makes demands on many subfunctions⁶ and it is difficult to identify the basis for poor performance from the single test score obtained. For example, lead workers have been reported to score lower than controls on the block design subtest from

the Wechsler Adult Intelligence Scale.¹ Consideration of the functions involved suggests that this result could be due to poor attentional control, impaired processing of visual spatial information, slow execution of responses, poor coordination, or tremor. Because performance in that subtest is reduced to a single score, it is not surprising that low scores have been variously interpreted as impaired psychomotor functioning⁴ or lower "visual intelligence."

In recognition of the many subfunctions contributing to performance in psychological tasks, tasks based on information processing theory have recently been selected to study neurotoxic effects.^{7,8} The main advantage of this approach is that it provides a systematic theoretical framework for the study of neurotoxic effects. This is a significant improvement over earlier work using standard intelligence scale items because it becomes possible to describe neurotoxic effects in terms of impairment to one or more processing stages. Although the postulated series of sequential processing stages is known to be an oversimplification,⁹ the approach has provided evidence that exposure to lead may impair the processes of encoding and response execution, in addition to the rate of scanning items in short term verbal memory.⁸

The present study sought to build up a profile⁶ of the

effects of exposure to lead on mood and major cognitive functions such as memory, attention, and verbal and spatial processing. The tasks selected were derived from publications on cognitive psychology^{3,9} and, as with work based on information processing theory, their theoretical basis provides a systematic framework for the establishment of a profile and the study of the nature of impairment found.

Design and protocol

SUBJECTS

The study population consisted of 91 male workers with varying degrees of exposure to inorganic lead: mean age 41.5 years (range 23–64). On the basis of their blood lead concentration at the time of testing, subjects were allocated to one of three lead groups: low (below 20 µg/dl), medium (21–40 µg/dl), and high (41–80 µg/dl). Subjects were recruited from local battery and printing industries and all spoke English as their first language. None had been treated for lead intoxication or had had blood lead concentrations exceeding 80 µg/dl in the preceding three years. The testing took place on site, in a quiet room, during normal work hours and subjects received their normal pay during participation.

DESIGN

Workers first attended a familiarisation session where they were informed of the study requirements, had any questions answered, completed a short practice session on the psychological tasks, and decided whether to participate in the main study. The main study design was longitudinal and volunteers normally agreed to participate in four testing sessions during the course of a year. The present paper reports the findings from a cross sectional analysis of the data—that is, data from the first session only.

LEAD ABSORPTION

Three measures of lead absorption were assayed concurrently with the cognitive testing: blood lead concentration, zinc protoporphyrin (ZPP), and urinary aminolaevulinic acid (ALA). As part of the study conditions, all subjects provided urine for ALA assays. Urinary ALA was measured using Biorad laboratory kits and corrected for creatinine. Blood was taken, by venepuncture (5 ml), on a voluntary basis and assayed for blood lead concentration and zinc protoporphyrin. Blood lead concentration was measured by atomic absorption spectrophotometry (Virian Spectra AA30) and ZPP was measured using an EGA haemofluorometer. Five lead workers who declined to provide blood samples were excluded from all data analyses reported here.

PSYCHOLOGICAL TASKS

Before starting the battery of psychological tasks, subjects completed a mood checklist assessing self reports of stress and arousal¹⁰ and a job checklist assessing self reports of work demands and discretion.¹¹ They also answered questions about their sleep habits, average weekly and recent alcohol consumption, previous exposure to lead, and age at leaving school.

The cognitive tasks were presented and controlled by a 380 Z microcomputer (Research Machines Ltd, Oxford) in a test session lasting about 25 minutes. The tasks were always performed in the following order: syntactic reasoning, serial reaction time, category search, visual spatial memory, and category search recall. Except in the serial reaction time task, stimuli were presented on a video monitor and responses were made by pressing either the T (true) or F (false) key on a standard keyboard. Subjects were asked to respond as quickly and accurately as possible using their dominant hand.

SYNTACTIC REASONING

Syntactic reasoning required subjects to verify a series of statements that claimed to describe the order of a pair of letters—for example, “A is followed by B. AB.” Statements were phrased in the active or passive voice, in a positive or negative form, and either correctly or incorrectly described the order of the letters.¹² In the analysis the six minute task was divided into three work periods of two minutes each.

SERIAL REACTION TIME

The apparatus for this sensory motor reaction time and attention task has been described elsewhere.¹³ Subjects extinguished one of five peripheral lights by touching its adjacent response disc (decision time) and initiated the next trial by touching a centre disc (movement time). A randomly varying delay of up to four seconds was introduced between the touching of the centre disc and the presentation of the next peripheral light. This delay was used to define four periods of waiting for light presentation: 0–1 s, 1–2 s, 2–3 s, and 3–4 s. In the analysis the nine minute task was divided into three work periods of three minutes each.

CATEGORY SEARCH

In this semantic classification task subjects decided whether a series of 80 nouns, presented individually at a self paced rate, were members of a semantic category (true/false). Two classification lists were constructed: (a) 20 category nouns mixed with 20 related distractors and (b) the same 20 category nouns mixed with 20 unrelated distractors. The two lists were presented without a break, in counterbalanced order, and each

subject saw the nouns in a new random sequence.

The category nouns comprised equal numbers of typical—for example, robin—and atypical—for example, grouse—members of the category “birds”^{14,15}; related distractors were other animal nouns—for example, spider—and unrelated distractors were high frequency inanimate nouns—for example, century.

VISUAL SPATIAL MEMORY

Visual spatial memory required the short term retention of spatial information. Up to six circles (the memory set) were shown at randomly selected positions inside a large square (19 × 19 cms) on the video monitor. One second after erasure of the memory set, a question mark probe was presented and the subject decided whether the probe was at a memory set location (true/false). Underlying the outline of the square was an invisible 9 × 9 grid system which defined 81 possible memory locations. Memory sets of two, four, and six locations were randomly selected for presentation and shown for two, three, and four seconds respectively—that is, presentation times were one second plus 0.5 seconds per memory item. Only one location was tested for recognition on each trial: a “true” probe occupied a randomly selected memory location and a “false” probe occupied one of the eight locations surrounding a randomly selected memory location. Subjects completed five replications of the resulting truth × memory set design, in a random sequence of trials, in about five minutes.

CATEGORY SEARCH RECALL

After the visual spatial memory task, subjects were given two minutes for the written free recall of any of the nouns they could remember from the category search task given earlier.

Table 1 Summary of the mean values on the group matching variables for 91 subjects differentially exposed to lead

	Low (n = 28)	Medium (n = 27)	High (n = 36)
Blood lead (µg/dl)	10.0	30.1	50.7
ZPP (µg/dl)	8.7	22.4	58.8
Urinary ALA (mg/l)	2.5	4.0	5.7
Years of lead exposure	4.8	11.7	9.0
Age (y)	46.2	41.1	38.2
Age left school (y)	15.3	15.4	15.5
Normal sleep (h)	7.2	7.3	7.0
Recent sleep (h)*	6.6	7.3	6.7
Weekly alcohol (ml)†	167.0	234.0	264.0
Recent alcohol (ml)*	8.0	24.0	36.0
Work demands‡	13.5	15.9	16.8
Work discretion‡	16.5	13.9	15.6
Stress score§	4.1	4.4	3.6
Arousal score§	8.8	7.7	8.0

*Value for past 24 hours.

†20 ml = 1 pint of beer.

‡Raw score from Karasek job questionnaire.¹¹

§Adjusted score from MacKay mood checklist.¹⁰

STATISTICAL ANALYSIS

Test scores were analysed using a repeated measures analysis of variance with covariance.¹⁶ The only grouping factor was the three levels of lead exposure (low-medium-high), the within subject factors were the cognitive task parameters, and the covariates comprised the non-exposure variables detailed in table 1. Before testing for effects due to lead exposure, the contribution of the non-exposure variables to performance scores was assessed and, when necessary, controlled by covariate analysis. The results of the covariate analysis are reported under the effects of factors other than exposure. Exposure response correlations were computed using multiple regression techniques.

Results

Table 1 shows the mean levels of exposure for the three groups: blood lead concentrations ranged from 5 to 72 µg/dl, ZPP from 7 to 210 µg/dl, and urinary ALA from 0.5 to 22 mg/l. The linear correlation between blood lead concentrations and ZPP was highly significant ($r = 0.57$, $F(1,77) = 36.4$, $p < 0.001$) but, not unexpectedly,¹⁷ there were several subjects who had high ZPPs (120–210 µg/dl) but moderate blood lead concentration (42–55 µg/dl).

Table 1 also shows the mean values for the three groups on several non-exposure variables. A series of one way analyses of variance showed that the groups differed on three of these variables. The high group reported more demanding work ($F(2,88) = 4.1$, $p < 0.05$), tended to be younger ($F(2,88) = 4.5$, $p < 0.05$), and had drunk more alcohol in the past 24 hours ($F(2,88) = 3.5$, $p < 0.05$) although they did not drink significantly more alcohol per week ($F(2,88) = 1.5$, $p = 0.22$).

MOOD CHECKLIST

After controlling for significant covariates, the three lead groups did not differ with regard to how stressed ($p = 0.66$) or aroused ($p = 0.28$) they felt. Multiple regression analysis showed an insignificant exposure response correlation between arousal and blood lead concentration ($p = 0.16$), ZPP ($p = 0.16$) and urinary ALA ($p = 0.54$). Failure to control covariates (see below), however, showed lower arousal scores for the high group ($p < 0.01$) and a negative correlation between arousal and blood lead concentration ($r = -0.26$, $p < 0.01$) but not ZPP ($p = 0.27$) or urinary ALA ($p = 0.23$).

EFFECTS OF OTHER FACTORS

Arousal was higher when subjects reported that their work was high in discretion ($r = 0.37$, $F(1,87) = 15.7$, $p < 0.01$) and low in demands ($r = -0.28$, $F(1,87) =$

Cognitive functioning in lead workers

9.1, $p < 0.01$). Arousal was also higher when stress was low ($r = -0.37$, $F(1,87) = 17.4$, $p < 0.001$) and vice versa ($r = -0.45$, $F(1,89) = 22.6$, $p < 0.001$).

When the influence of covariates was not controlled the three groups differed in arousal ($F(2,88) = 5.2$, $p = 0.007$) and the blood lead correlation was significant ($r = -0.26$, $F(1,88) = 6.6$, $p = 0.01$). Stepwise multiple regression showed that arousal and blood lead concentration remained correlated after stress ($r = -0.24$, $F(1,88) = 6.6$, $p = 0.01$) and work discretion ($r = -0.20$, $F(1,87) = 5.2$, $p = 0.02$) were controlled, but not after work demands were controlled ($r = -0.13$, $F(1,86) = 2.0$, $p = 0.16$); as reported above. That is, the type of work performed by the high group differed from the work of others in ways that had nothing to do with exposure to lead. These differences, rather than the lead, were associated with differences in arousal.

Although lower arousal levels have been associated with higher work demands in other populations,¹⁸ in this study it was possible that controlling for the influence of arousal on performance might remove potential lead effects because of the intercorrelations between work demands, arousal, and blood lead concentrations. Low arousal, as reported by the worker, might be a dependent rather than independent variable. It was decided, therefore, that whereas it was legitimate to control for effects on performance due to work demands, the effects on performance due to arousal would not initially be controlled.

SYNTACTIC REASONING

Table 2 summarises the overall speed and accuracy of syntactic reasoning for the three groups. There was a tendency for the high group to attempt fewer trials ($F(2,88) = 2.4$, $p = 0.09$) and for that score to be correlated also with blood lead concentrations ($r = -0.17$, $F(1,89) = 2.8$, $p = 0.09$), but neither result reached satisfactory levels of statistical significance.

Table 2 Overall levels of performance in the syntactic reasoning task as a function of exposure to lead

	Lead group		
	Low	Medium	High
Overall analysis (n = 91):			
Total trials attempted*	64.2	58.5	54.2
No of errors	6.9	12.8	12.1
Correct reaction time (s)	5.0	5.2	5.7
Reaction time variability (s)†	2.4	2.3	2.4
Overall accuracy (%)	89.0	85.0	85.0
Linguistic analysis (n = 79):			
Correct reaction time (s)	4.9	5.0	5.8
Overall accuracy (%)	90.0	88.0	91.0

*Including errors.

†Standard deviation of correct reaction time.

The groups did not differ on the mean number of errors made ($p = 0.46$), correct reaction time ($p = 0.33$), accuracy ($p = 0.57$), or the variability (SD) of correct reaction times ($p = 0.96$). For none of these measures did the correlations with blood lead concentration, ZPP, and urinary ALA approach significance. Controlling for the influence of arousal on the number of trials attempted eliminated the correlation with individual blood lead concentration (see below).

Reasoning speed and accuracy was also examined with respect to the linguistic structure of the reasoning problems. Unfortunately, one subject in the low group, three in the medium group, and eight in the high group had 0% accuracy on certain problems (mainly passive). Owing to the resulting missing correct reaction time data, the results from those 12 subjects were excluded from the linguistic analysis. Accuracy scores were analysed using the arcsine transformation.

As has been found in earlier studies,^{12 19 20} some of the problems within the task were harder than others, and it was desirable to examine the extent to which this made them more or less vulnerable to lead. Across all groups, problems took progressively longer to verify, and were verified less accurately, in the following order: active-positive, passive-positive, active-negative, and passive-negative (all $p < 0.001$). The truth x negation interaction for speed ($p < 0.001$) and accuracy ($p < 0.01$) showed that positive statements were easier when they correctly described the letters, whereas negative statements were easier when they incorrectly described the letters.

The difficulty of individual problems had a suggestive but borderline significant relation to the size of the difference between groups. That is, the truth x voice x negation x group interaction gave $F(2,76) = 2.7$, $p = 0.08$. The speed of answering the problems was roughly equivalent for the low and medium groups, but the high group took progressively longer to verify false statements of increasing difficulty (fig 1). A re-analysis of the linguistic accuracy data, which included the 12 subjects with missing reaction time data, did not show any significant effect of exposure to lead on accuracy.

EFFECTS OF OTHER FACTORS

Accuracy was lower when stress was high ($r = 0.42$, $F(1,77) = 16.2$, $p < 0.001$) and responses were faster when arousal was high ($r = -0.34$, $F(1,77) = 10.2$, $p = 0.002$). As noted above, the inclusion of arousal as a covariate eliminated the correlation between individual blood lead concentration and the number of trials attempted ($r = -0.10$, $p = 0.34$) but otherwise it did not affect the findings reported above.

Fig 1 Speed of verifying syntactic reasoning problems as function of statement complexity and exposure to lead ($p = 0.08$). Active-positive (AP), passive-positive (PP), active-negative (AN), and passive-negative (PN).

CATEGORY SEARCH AND FREE RECALL

Original classification of nouns at time of presentation
Table 3 shows that the high group took longer to classify distractor nouns ($F(2,88) = 3.9$, $p = 0.03$) and category nouns ($F(2,88) = 3.8$, $p = 0.03$). The blood lead correlation was significant for both distractor ($r = 0.23$, $F(1,89) = 4.8$, $p = 0.03$) and category ($r = 0.22$, $F(1,89) = 4.6$, $p = 0.03$) nouns. None of the correlations with ZPP and urinary ALA was significant.

In this task also different aspects of the task were of different difficulty. Across all groups: (a) related distractors were rejected more slowly than unrelated distractors ($F(1,88) = 45.2$, $p < 0.001$), (b) related distractors were rejected less accurately than unrelated distractors ($F(1,88) = 81.2$, $p < 0.001$), (c) among the nouns which were accepted, on the other hand, "typical" members of the category were classified more quickly ($F(1,88) = 27.2$, $p < 0.001$) and more accurately ($F(1,88) = 30.2$, $p < 0.001$) than "atypical" members, and (d) accepted nouns were also classified more slowly when the other distractor nouns with which they were mixed were related rather than

Table 3 Overall classification speed (ms) and accuracy (%) in the category search task as a function of exposure to lead. (Accuracy in parentheses)

Noun classification	Type of distractor	Lead group		
		Low	Medium	High
Category	Unrelated	924 (99.6)	965 (99.6)	1157 (98.9)
	Related	1009 (99.6)	1100 (98.7)	1207 (98.1)
Distractor	Unrelated	1032 (99.7)	1112 (99.9)	1345 (99.8)
	Related	1318 (94.5)	1309 (97.5)	1478 (96.6)

unrelated ($F(1,88) = 15.9$, $p < 0.001$), and this slowing was greater if the accepted noun was atypical ($F(1,88) = 5.1$, $p = 0.03$).

Again, the relation of lead effects to difficulty was ambiguous. Of the four sources of difficulty mentioned, source (a) did not differ significantly between the groups (group $\times$ distractor type interaction gives $F(2,88) = 2.2$, $p = 0.12$). Yet the correlation with individual blood lead concentration was significant for unrelated distractors ($r = 0.34$, $F(1,89) = 11.3$, $p < 0.001$) but insignificant for related ones ($r = 0.11$, $p = 0.31$): the difference in the strengths of the correlations being significant ($T = 3.41$, $p < 0.01$). For source (b) the high group tended to reject all distractors more accurately ($F(2,88) = 3.1$, $p = 0.05$), the correlation between overall accuracy and individual blood lead concentration was insignificant ($r = 0.15$, $F(1,89) = 2.0$, $p = 0.16$), and the effect of distractor difficulty did not differ significantly between the groups ($p = 0.56$). For source (c), atypical members gave a significant correlation between individual blood lead concentration and speed ($r = 0.24$, $F(1,89) = 5.3$, $p = 0.02$) although not accuracy ($r = -0.11$, $F(1,89) = 1.1$, $p = 0.29$). Typical members gave a borderline significant correlation with speed ($r = -0.18$, $F(1,89) = 3.1$, $p = 0.08$) and also with accuracy ($r = -0.18$, $F(1,89) = 3.1$, $p = 0.08$). For source (d), there was no change in the effect of difficulty as lead exposure increased ($F(2,88) = 1.34$, $p = 0.27$). None of the correlations with ZPP and urinary ALA was significant.

Results on the delayed free recall of all nouns

Table 4 shows the delayed free recall scores for the three groups. For those nouns that were correctly recalled, the four different types of noun differed substantially in their ease of recall, with recall levels declining progressively in the following order: typical instances, atypical instances, related distractors, and unrelated distractors ($F(3,264) = 115.2$, $p < 0.001$). More specifically: (a) for nouns which were members of the category, typical members were recalled better than atypical members ($F(1,88) = 12.5$, $p < 0.001$); (b) for nouns which were not members of the category,

Table 4 The number and type of nouns recalled from the category search task as a function of exposure to lead

	Lead group		
	Low	Medium	High
Typical instance	4.18	4.18	4.36
Atypical instance	3.46	3.52	3.47
Related distractor	2.07	1.88	1.48
Unrelated distractor	1.28	0.88	0.65
Intrusion error	0.00	0.04	0.03
Extra list error	1.11	0.93	0.86

those related to it were recalled better than those which were unrelated to it ($F(1,87) = 21.8, p < 0.001$).

The relation of the effects of lead to the above sources of difficulty was not clear. For source (a), the three groups recalled equivalent numbers of category nouns ($p = 0.93$) and the effect of difficulty did not interact with groups ($p = 0.90$). For source (b), however, the high group recalled numerically fewer distractor nouns overall ($F(2,87) = 2.23, p = 0.11$) and the correlation with individual blood lead concentration was of borderline significance ($r = -0.21, F(1,88) = 3.7, p = 0.06$). Yet, although the effect of difficulty noted in source (b) did not differ as a function of groups (the group $\times$ distractor type interaction gave $F < 1$), the correlation with individual blood lead concentration was significant for unrelated nouns ($r = -0.22, F(1,88) = 4.0, p = 0.049$) and insignificant for related nouns ($r = -0.14, F(1,88) = 1.7, p = 0.20$): the difference in the strengths of the correlations not being significant ($T = 0.7, p > 0.25$). Thus whereas there appears to be some evidence that the recall of distractor nouns was in general poorer when blood lead concentration was high, the evidence pointing to a particular difficulty with unrelated distractors does not reach satisfactory levels of significance. None of the correlations was significant for ZPP and urinary ALA.

Although recall errors were rarely made, extra list errors (nouns not shown) were produced more often than intrusion errors (nouns seen at familiarisation): $F(1,88) = 81.2, p < 0.001$. The extra list error rate was not correlated with blood lead concentration, ZPP, or urinary ALA. The intrusion error rate was positively correlated with urinary ALA ($r = 0.29, p = 0.005$), but not with blood lead concentration ($r = 0.03, p = 0.77$) or ZPP ($r = 0.09, p = 0.38$).

Effects of other factors

Older subjects recalled fewer distractor nouns ($r = -0.23, F(1,89) = 4.8, p = 0.03$) but an equivalent number of category nouns ($r = -0.11, p = 0.29$)—that is, age affected the recall of nouns that were not being searched for in the classification task. Intrusion errors tended to be produced more frequently when work demands were high ($r = 0.20, F(1,88) = 3.7, p = 0.06$) and when stress was high ($r = 0.18, F(1,88) = 2.9, p = 0.09$).

SERIAL REACTION TIME

Table 5 summarises the overall speed, accuracy, and gap rates in the serial reaction time task. Concentration lapses were examined by counting the incidence of slow correct reaction times or gaps^{13,21,22} during the decision phase (decision gaps) and the movement phase (movement gaps) of the task. As the percentage

Table 5 Overall performance in the serial reaction time task as a function of exposure to lead

	Lead group		
	Low	Medium	High
Total attempted*	480.6	488.7	459.9
Error rate (%)	2.6	3.3	2.9
Decision time (ms)	707	693	807
Decision variability (ms)	158	138	193
Movement time (ms)	297	302	340
Movement variability (ms)	45	39	41
Decision gaps (%)	10.0	8.5	12.5
Movement gaps (%)	1.0	1.1	1.0

*Including errors.

of trials on which gaps occurred was low, the arcsine transformation was applied.

The high group attempted fewer trials ($F(2,86) = 4.9, p < 0.01$) and the correlation with individual blood lead concentration was significant ($r = -0.21, F(1,86) = 4.4, p = 0.04$). This slower performance by the high group was most apparent on decision times ($F(2,85) = 5.9, p = 0.004$), which also showed a significant correlation with individual blood lead concentrations ($r = 0.25, F(1,86) = 6.4, p = 0.01$) but not ZPP ($r = 0.15, p = 0.15, p = 0.14$) or urinary ALA ($r = 0.07, p = 0.46$). The standard deviation of decision times (decision variability) was also greater in the high group ($F(2,86) = 4.5, p = 0.01$) and although the correlation with blood lead concentration did not achieve significance ($r = 0.17, p = 0.10$), the correlation with ZPP did ($r = 0.21, p = 0.05$). The movement times of the high group were numerically slower than those of the other groups ($F(2,87) = 2.6, p = 0.08$) and were significantly correlated with individual blood lead concentration ($r = 0.22, F(1,88) = 4.1, p = 0.04$) but not with ZPP ($p = 0.77$) or urinary ALA ($p = 0.97$). The standard deviation of movement times

Fig 2 Movement times in serial reaction time task as function of task duration and exposure to lead ($p = 0.02$).

(movement variability) was equivalent for the three groups ($p = 0.34$) and none of the exposure response correlations was significant. As shown in fig 2, the movement times of the low group remained at a stable level throughout the nine minute task, but the medium and high groups showed some improvement during the first few minutes ($F(4,176) = 2.9$, $p = 0.02$).

The duration of waiting for light presentation had a major impact on serial reaction time performance. Decision times were slowest and decision gaps occurred most often after the shortest waiting period (0–1 s), whereas movement times were slowest and movement gaps occurred most often after the longest waiting period (3–4 s): all $p < 0.001$. For decision times, the size of the difference between groups was not influenced by the waiting period ($p = 0.44$) and multiple regression analyses confirmed that individual blood lead concentration was correlated with decision times at each waiting period (0–1 s: $r = 0.27$, $p = 0.01$; 1–2 s: $r = 0.24$, $p = 0.02$; 2–3 s: $r = 0.23$, $p = 0.03$; 3–4 s: $r = 0.24$, $p = 0.02$). Similarly, for movement times, the difference between groups was independent of the waiting period ($p = 0.40$) and individual blood lead concentration was correlated with movement times at each waiting period (0–1 s: $r = 0.22$, $p = 0.04$; 1–2 s: $r = 0.23$, $p = 0.04$; 2–3 s: $r = 0.21$, $p = 0.05$; 3–4 s: $r = 0.21$, $p = 0.05$). The only other correlation approaching significance was between ZPP and decision times at the shortest period of waiting ($r = 0.17$, $p = 0.08$).

The movement gap rates of the three groups were identical ($p = 0.93$) but the high group had a higher decision gap rate ($F(2,87) = 3.3$, $p = 0.04$). The overall decision gap rate was not correlated with blood lead concentration ($r = 0.17$, $F(1,88) = 2.6$, $p = 0.11$), ZPP ($p = 0.38$), or urinary ALA ($p = 0.54$). Although the interaction between the waiting period and lead groups was not significant ($F(6,264) = 1.4$, $p = 0.23$), multiple regression showed a significant correlation between individual blood lead concentration and decision gaps at the shortest period of waiting (0–1 s: $r = 0.26$, $F(1,88) = 6.6$, $p = 0.01$), a just significant correlation for the next longest period of waiting (1–2 s: $r = 0.19$, $F(1,88) = 3.5$, $p = 0.06$), and insignificant correlations for longer periods of waiting (2–3 s: $r = 0.07$, $p = 0.55$; 3–4 s: $r = -0.03$, $p = 0.78$). A comparison of the strengths of the blood lead correlations at the shortest (0–1 s) and longest (3–4 s) periods of waiting showed that they differed significantly ($T = 2.82$, $p < 0.01$). The correlation between ZPP and decision gaps was at, or near, conventional significance for the two shortest periods of waiting (0–1 s: $r = 0.18$, $p = 0.09$; 1–2 s: $r = 0.23$, $p = 0.03$). None of the correlations with urinary ALA was significant.

Effects of other factors

Age influenced many aspects of performance. Older

subjects had longer ($r = 0.28$, $F(1,85) = 11.3$, $p < 0.001$) and more variable ($r = 0.20$, $F(1,88) = 4.3$, $p = 0.04$) decision times, longer movement times ($r = 0.21$, $F(1,87) = 6.5$, $p = 0.01$), made more errors ($r = 0.25$, $F(1,89) = 6.0$, $p = 0.02$), and had a higher decision gap rate ($r = 0.36$, $F(1,87) = 13.5$, $p < 0.001$). In addition, when self reported stress was high, decision times were slower ($r = 0.28$, $F(1,85) = 8.6$, $p < 0.01$) and more variable ($r = 0.32$, $F(1,88) = 10.5$, $p = 0.002$). Decision times were also slower when work autonomy or discretion was high ($r = 0.24$, $F(1,85) = 5.4$, $p < 0.05$). It is worth reiterating that all of the above non-exposure variables were controlled before testing for effects due to lead exposure.

VISUAL SPATIAL MEMORY

Two subjects in the low group had 0% accuracy for the largest memory set and, because of the missing correct reaction time data for that condition, their results had to be excluded from analysis. The remaining 89 subjects correctly recognised the position of the probe in an average of 1.38 s with an overall accuracy of 84%. Accuracy scores were analysed using the arcsine transformation.

Table 6 shows the overall recognition speed and accuracy in the visual spatial memory task. After controlling for significant covariates, the three groups did not differ in terms of speed ($F(2,84) = 2.4$, $p = 0.10$) and the correlations with individual blood lead concentration ($r = -0.17$, $F(1,85) = 2.3$, $p = 0.13$), ZPP ($p = 0.24$) and urinary ALA ($p = 0.69$) were insignificant. The blood correlation, however, was significant when the covariates were not controlled ($r = -0.22$, $p = 0.05$). With respect to accuracy, the three groups performed equivalently ($p = 0.64$) and none of the exposure-response correlations was significant.

Increasing the number of locations to remember (memory set) resulted in slower ($F(2,172) = 19.6$, $p < 0.001$) and less accurate ($F(2,172) = 61.3$, $p < 0.001$) recognition; with accuracy declining faster for probes shown in "false" locations (truth $\times$ memory set interaction ($F(2,172) = 5.3$, $p < 0.01$). There was no evidence for impaired visual spatial memory because the three lead groups had equivalent patterns of

Table 6 Recognition speed (ms) and accuracy (%) in visual spatial memory task as a function of exposure to lead ($n = 89$). (Accuracy in parentheses)

Memory set*	Lead group		
	Low	Medium	High
2	1166 (96)	1197 (95)	1389 (95)
4	1348 (81)	1330 (81)	1397 (79)
6	1448 (77)	1417 (75)	1597 (69)

*Number of positions to remember.

performance on the task. A reanalysis of the accuracy data, which included the two subjects with missing correct reaction time data, showed no effects from exposure to lead.

Effects of other factors

Older men had longer recognition times ($r = 0.26$, $F(1,86) = 6.7$, $p = 0.01$) as did those reporting more demanding work ($r = 0.25$, $F(1,86) = 6.2$, $p = 0.02$). Recognition speed and individual blood lead concentration were significantly correlated after controlling for age ($r = -0.22$, $F(1,86) = 4.1$, $p = 0.05$) but not after controlling for age and work demands ($r = -0.17$, $p = 0.13$) as reported above.

Discussion

The results reported here support the view that occupational exposure to inorganic lead may impair performance on a range of cognitive tasks and they go some way toward specifying which functions contribute to the impaired performance. Workers with blood lead concentrations above 40 $\mu\text{g}/\text{dl}$ (high group) showed clear evidence of impairment on tests of serial reaction time and category search, with only weak evidence of impairment being observed on tasks probing syntactic reasoning and delayed verbal free recall. In general, the magnitude of these impairments correlates better with measures of blood lead concentration than with ZPP or urinary ALA. By contrast, exposure to lead does not appear to affect self reports of stress and arousal, or performance in a visual spatial memory task.

The clearest evidence of impairment was observed in the serial reaction time task. After controlling for the effects of significant non-exposure factors, individual blood lead concentrations correlated positively with both decision and movement times. In functional terms this result may be characterised as a general slowing of sensory motor reaction time. The non-specific nature of this slowing is indicated by two types of evidence. Firstly, decision times (light detection, response selection, and execution) are slowed more than movement times (response execution) implicating impaired sensory encoding as well as impaired motor responses. Secondly the degree of lead induced impairment is not modified by task factors which have a clear influence on the speed of decision making—for example, the period of waiting for light presentation—and therefore the impairment appears to be independent of decision processes per se. In addition to this slowing, transitory moments of inefficiency in light detection (decision gaps) also tend to be more common in workers with high blood lead concentrations. Since there was some evidence that these moments of inefficiency correlate better with

individual blood lead concentrations at short periods of waiting, this suggests that the more exposed workers had poorer attentional control when the attentional demands of the task were great. That is, that task showed evidence for both sensory motor slowing and impaired attention.

Category search performance was also clearly impaired by exposure to lead; the speed of classifying category nouns and distractor nouns was negatively correlated with blood lead concentration. The stronger correlation for atypical, compared with typical, category members might initially be regarded as evidence that the more difficult category classifications showed more consistent slowing. When accuracy scores are considered, however, a speed accuracy trade off is implicated: typical members are classified less accurately with increasing blood lead concentration but atypical members show no such relation. Taken together, these findings suggest that the processing of category information is not impaired and point to the involvement of more peripheral functions in the underlying impairment—for example, stimulus encoding, response selection, and motor execution. Thus in common with the results from the serial reaction time task these findings may also be understood in terms of a non-specific slowing of sensory motor reaction time.

A comparison of the strengths of the blood lead correlations for the two types of distractors adds a slight complication to the hypothesis that exposure to lead leads to a simple slowing of sensory motor functions. Although unrelated distractors proved easier to reject than related distractors, blood lead concentration tended to correlate better with the speed of rejecting the easier unrelated distractors. In theoretical terms this result might suggest that workers with higher blood lead concentrations were placing less reliance on the initial fast, holistic stage of categorisation that has been postulated for rejecting items with a low semantic relatedness to the search category.¹⁴ This explanation is also consistent with the speed accuracy trade off found for typical members because the initial fast categorisation process is also mainly involved in the acceptance of items with a high semantic relatedness to the search category.¹⁴

Whereas the above results indicate that inorganic lead exerts its major influence on the sensory motor component of various cognitive tasks, there is some subsidiary evidence pointing to mild impairment of verbal processing and memory. Firstly, in the syntactic reasoning task the high group tended to take disproportionately longer to answer the more difficult problems and the interaction with problem complexity suggests the involvement of cognitive rather than merely sensory motor functions. This verbal reasoning task has also been used to explore subcomponents of

working memory¹⁹ and on the basis of that research the results imply a reduction of central processing resources for the more exposed workers. Secondly, selective impairment in the recall of verbal material is indicated by the lead workers' free recall profile: normal recall for category nouns and related distractor nouns but poorer recall for the most difficult nouns to remember (unrelated distractors). This memory impairment, which reflects a difficulty in accessing information that is poorly related to the focus of the category search, cannot be due to shorter item inspection times because the more exposed workers actually took longer to reject the unrelated distractors. This evidence for impairment of verbal processing and memory functions, however, is less compelling than the evidence for sensory motor impairments.

Only the visual spatial memory task did not show clear evidence of a lead induced impairment. In this case acceptance of the null hypothesis was critically dependent on the appropriate control of self reported work demands because otherwise the correlation between blood lead concentration and recognition speed was significant. Although the more exposed workers reported higher levels of perceived work demands, it is difficult to determine in this study whether this is due to their exposure to lead or to the nature of the work where exposure to lead occurs. Even when the effects of work demands were not controlled, however, the performance profile failed to show evidence for impaired visual spatial memory and processing, and simply provided further evidence for a general slowing that was independent of cognitive parameters—for instance, memory set size.

In conclusion, the main weight of evidence in the present study suggests that it is the sensory motor, rather than cognitive, requirements of many psychological tasks that provide the most sensitive index of the early effects of chronic low level lead exposure. This explanation accords with earlier evidence of slower performance by lead workers on a variety of psychological tasks.^{4,5,8,23,24} Unfortunately, many of the earlier studies have tended to interpret evidence of test impairment as the disruption of most, if not all, of the psychological functions that contribute to test performance often by describing it in terms of multifunctional concepts such as "intelligence." The results presented here suggest that much of this evidence for impairment may be identified with the sensory motor demands common to the various tasks. As was noted above, psychological performance in any particular task requires the cooperation of many functions and single performance measures do not permit choices to be made between competing interpretations for the locus of functional impairment. Tasks chosen from the performance (non-verbal) scale of the Wechsler Adult Intelligence Scale (WAIS) are particularly

problematical in this respect. In addition to the various visual spatial demands made by each performance subtest of the WAIS, the subtests also share a significant motor component. Given the standard scoring practice of allocating extra marks for fast correct performance, with no points if correct performance cannot be achieved within a certain time limit, scores naturally tend to emphasise speed. This makes it difficult to specify which psychological functions contribute most to poorer test scores, a difficulty which becomes especially acute when impaired sensory motor functioning is suspected. The more detailed analysis of task performance undertaken here does permit the various functional impairments to be separated and described more clearly, and this approach appears capable of providing continued insights into the nature and mechanisms of impairments produced by neurotoxic agents.

At a more general level, previous research with serial reaction time tasks suggests that inorganic lead may be broadly classified with drugs such as barbiturates, alcohol, and diazepam, which also exert their major influence on the average speed of performance. It has been pointed out elsewhere that the underlying neurochemical basis for this slowing may be the receptor sites modulating the postsynaptic response to the inhibitory neurotransmitter gamma-aminobutyric acid (GABA).²⁵ As ample evidence exists for an effect of lead on the GABAergic system,²⁶⁻²⁸ this opens up the possibility that the correlation between average speed and blood lead concentration might actually reflect underlying changes in GABAergic neurotransmission. There is also growing evidence that lead may modify the normal functioning of both the cholinergic and also the dopaminergic systems²⁹⁻³¹ (and MJ McIntosh, unpublished data). The finding that transient periods of inefficiency in serial reaction time, as well as slower average speed, tended to be more common with increasing blood lead concentration suggests that the effects have similarities, not only to those produced by barbiturates, alcohol, and diazepam but also to those characteristic of the system affected by chlorpromazine and amphetamine. Since the latter drugs are thought to affect receptor sites for dopamine,^{25,31} disruption to the dopaminergic system may possibly form the basis for the attentional difficulties suggested by the present results.³²

The observation that some biochemical indicators of lead absorption (such as blood lead concentrations) correlate strongly with performance impairments whereas others, ZPP and urinary ALA, do not, raises the possibility that the different indices may be related in various ways to underlying changes in neurotransmitter function. The link between biochemical measures of absorption and neuronal transmission,

however, is at best indirect and complex,²⁶ and it is not surprising that efforts to establish correlations between performance and biochemical dysfunction have met and are likely to continue to meet with mixed success. Finally, the range of neurochemical system affected by exposure to lead suggests that lead induced impairments in psychological tasks are unlikely to be entirely accounted for by the disruption of a single transmitter system. It seems more plausible to hypothesise that each neurochemical system makes its own contribution to the profile of impaired psychological functioning. Notwithstanding the paucity of available information concerning the relation of neurochemical systems to psychological performance,³³ the parallel classification scheme may prove to be an important tool for studying the nature of the basis for the lead induced impairments found using psychological tests. More peripheral sources, however, such as the reductions in motor nerve conduction velocities that accompany low level lead exposure,² should not be overlooked as a basis for the sensory motor slowing found in this and other studies of workers exposed to lead.

This work was supported by the Commission of European Communities and the Health and Safety Executive (UK). We thank the workers for their participation and the management and trade unions for their help in coordinating the testing. We gratefully acknowledge the help of the factory occupational health departments in collecting samples and the National Occupational Hygiene Service for the analysis of samples.

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