Decrements in cognitive performance in metal inert gas welders exposed to aluminium

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Abstract
Objectives—**Often little has been discovered of the cognitive functions affected by occupational toxins because many functions cooperate to produce the single performance scores typically reported from neuropsychological tests. To facilitate the interpretation of neuropsychological scores, the issue of occupational exposure to aluminium was examined with an approach intended to increase understanding of those cognitive processes that may be affected.**
Methods—**The investigation was a cross sectional study of asymptomatic aluminium welders and a reference group of mild steel welders. Based on urinary aluminium concentrations, welders were classified into a reference (n=28), low (n=27), and high (n=24) exposure group. The mean urinary aluminium concentrations were 0.46, 2.25, and 9.98 µmol/l, respectively. A comprehensive neuropsychological examination was undertaken to assess psychomotor function, simple visual reaction time, attention related tasks, verbal and visual or visuospatial abilities as well as verbal and visual learning and memory.**
Results—**Aluminium welders showed no impairment on the finger tapping, Santa Ana dexterity, simple visual reaction times, any of the verbal memory tasks, the similarities subtest of Wechsler adult intelligence scale, or the Stroop task. However, the low exposed group performed poorer on the memory for designs and on more difficult block design items demanding preliminary visuospatial analysis. The time limited synonym task, embedded figures, digit symbol speed, and the backward counting component of the divided attention task showed exposure-response relations.**
Conclusions—**The impairments found were circumscribed. When the neuropsychological tasks were scored to show some of the underlying theoretical cognitive structures, the results indicated that performance difficulties were mainly detected in tasks requiring working memory, particularly that relating to processing of visuospatial information. There was also evidence that such impairments are more readily found in time limited tasks involving visually presented material, in which effective visual scanning combined with control of working memory is demanded.**
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There are only a few studies on the influence of occupational exposure to aluminium on a worker's cognitive performance. A diverse range of cognitive deficits including visuomotor or visuospatial problems,[1 2] attention deficits,[1 3] impaired verbal or visual memory and learning,[1 3 5] and problems with "concept formation"[1] have been reported. Two recent studies,[6 7] however, found no evidence of cognitive impairment associated with exposure and taken together, the various studies have not shown a high degree of consistency in the cognitive domains affected.

Variation in findings may be due to differences in the methods of assessment and the magnitude of exposure to aluminium. Certain methodological weaknesses have made it difficult to identify the role of aluminium in some of the conclusions drawn. For example, workers have been exposed to several potential toxicants other than aluminium,[4 5] no measures of aluminium uptake or body burden were reported,[4 5 8] no reference groups were used,[3 5] or findings based on very small samples have been reported.[9] The workers studied have been aluminium production workers employed in either the foundry or potroom[1 2 4 5 7 9] and aluminium welders[3 6] with normal, slightly, or moderately increased measures of body burden of aluminium. Among industrially exposed workers, welders who use the metal inert gas (MIG) technique have the highest concentrations of aluminium in urine and serum.[10 11]

Nevertheless, it is acknowledged that exposure to aluminium might impair cognitive performance with deficits in memory, attention, visuomotor, or visuospatial ability being the most likely functions to be impaired.[1 3] Although plausible, these suggestions about the functional locus of the aluminium deficits remain underspecified because a broad classification—such as deficits in memory—can refer to impairments on a wide range of tasks—for example, digit span, serial word learning, paired associate learning, recognition or reproduction of figural designs, sentence repetition, or recalling a complex story. Moreover, from a theoretical, diagnostic, or safety viewpoint such broad classifications are not informative. Memory is neither a unitary, nor a functionally isolated system but reflects the integrative output of many cognitive processes. Thus, an observed memory impairment can arise for several reasons. To deal with these issues, many authors have emphasised that the development of neurobehavioural test methods

requires more theoretically based measures to understand and evaluate the results from different studies.[12–16] The focus of this approach is on the characterisation of the impairment by attempting to specify those cognitive processes that contribute to the performance and its decrement.

The aim of this study was to describe more explicitly the putative effects of aluminium on cognitive abilities. In the present paper, neuropsychological data from a larger study on the functioning of the central nervous system of welders with up to 23 years of experience in metal inert gas aluminium welding are presented. To understand better the characteristics of any subtle deficits and their relation to exposure to aluminium, the neuropsychological data were scored, where possible, to show some of the underlying theoretical constructs. This was achieved by partitioning performance scores according to important task variables, such as item difficulty, rather than using standard scoring systems that usually summarise performance as a single score.

Methods

RECRUITMENT, PARTICIPANTS, AND EXPOSURE MEASURES

Based on sales data of welding materials, 10 companies with a long history of aluminium welding with the MIG technique were identified. The company management was contacted, and in each case they agreed to collaborate. Eight of the companies were small, each employing only a few aluminium welders. Two companies were larger, employing both aluminium and mild steel welders. A toxicologist and an industrial hygienist visited each company to make a survey to ensure that the workers were not exposed to other neurotoxic substances, and to inform the prospective volunteer welders, the management, and the occupational health organisation about the study. In the small companies, all welders who were currently welding with aluminium volunteered for the study. In the two larger companies, occupational health nurses contacted the aluminium welders and an age matched group of mild steel welders (referent group), and only a few refused to participate. Two thirds of the workers were tested at the Institute, whereas the biggest company preferred to provide testing premises at their own occupational health centre. Altogether 11 aluminium welders and 20 mild steel welders were tested at the workplace.

The ethical board of the Finnish Institute of Occupational Health approved the study protocol. All participants gave written informed consent. Before neuropsychological evaluation, the workers underwent a semistructural interview by a physician. The interview provided details on education, occupational history, past and present exposure to neurotoxic agents, past and present diseases, injuries, clinical symptoms, medication (including antacids containing aluminium) and smoking habits, as well as questions about general health, job satisfaction, and the frequency of use of respiratory protection. Alcohol use was estimated by asking workers for their average monthly consumption of beer, wine, and spirits. This was converted into common units of litres of 100% alcohol. All except one worker had secondary education, and many of the younger workers had additional professional training of 2–3 years.

A graphite furnace atomic absorption spectrometry method with Zeeman background correction was used to measure aluminium concentrations in urine and serum, and urinary aluminium concentrations were corrected to a relative density of 1.024. For serum analysis, the matrix matched standard curve was prepared and for urine the method of standard additions was used.[17] Urine samples were collected after two consecutive exposure free days, and blood samples were taken in the morning of the test day. Blood lead concentrations, taken to exclude one possible confounder, were all within the normal range (0.1–0.4 µmol/l).

From the original sample of 90, the application of several exclusion criteria—for example, neurological illness, previous exposure to other neurotoxic agents, possible primary learning disabilities, native language other than Finnish or Swedish—resulted in a sample of 82. Only one worker was excluded because of an abnormal neurological finding, but there was no suggestion that this was associated with exposure to aluminium (probable familial hemiataxia). There were no heavy drinkers in the study group and there was no reported use of antacids containing aluminium during the preceding month.

The workers were classified into three groups based on their urinary aluminium concentrations: reference (<1.0 µmol/l), low exposure (1.1–4.0 µmol/l), and high exposure (>4.1 µmol/l). However, because all the female welders (n=3) belonged to the high exposure group, they were excluded from the following analyses. The mean age of the remaining 79 male workers was 38.4 (range 22–58). The reference value for urinary aluminium in occupationally non-exposed populations is 0.6 µmol/l.[17]

Table 1 shows the characteristics of the three groups in terms of age, education, alcohol, and the two exposure indices. There were no differences between the groups for alcohol consumption (p =0.513) or education (p=0.396), but the high exposure group tended to be slightly older than the other two groups: $F(2,78)=3.0$, p=0.055. Age was positively correlated with both urinary ($r=0.267$, p=0.017) and serum ($r=0.349$, p=0.002) aluminium, and alcohol consumption correlated with urinary aluminium ($r=0.264$, p=0.019). Urine and serum aluminium levels were highly correlated ($r=0.802$, p<0.001).

Table 1   Mean (SEM) demographic data and exposure indices for the three exposed groups

Variable	Referent (n=28)	Low exposure (n=27)	High exposure (n=24)
Age (y)	37.62 (0.98)	36.75 (1.35)	41.33 (1.77)
Education (y)	9.86 (0.24)	9.96 (0.25)	9.42 (0.39)
Alcohol consumption*	0.54 (0.07)	0.43 (0.08)	0.56 (0.10)
Serum alcohol (µmol/l)	0.09 (0.01)	0.17 (0.01)	0.53 (0.04)
Urinary alcohol (µmol/l)	0.46 (0.04)	2.25 (0.17)	9.98 (1.16)

*Litres of 100% alcohol/month.

Table 2   Main cognitive domains assessed and the summary of the measures used in the neuropsychological tasks

Main cognitive domain	Neuropsychological task	Dependent variables
Psychomotor function	Finger tapping speed	Average of three sets (10s each)
	Santa Ana dexterity test	Sum of two sets (30s each)
	Simple visual RT	Mean reaction time and SD (6 min)
Attention	WAIS-R: digit span	Actual forward and backward span
	WAIS: digit symbol	Number attempted (90s)
	Stroop colour word test	Work rates and accuracy (40s)
	Dual task	Work rates and accuracy per minute, divided attention costs
Verbal abilities	WAIS: similarities	Total score (13 pairs): correct (2 points), adequate (1 point)
	Synonyms	Item selection time and accuracy (6 min)
Visuospatial skills	Embedded figures	Correct identifications (max 40)
	WAIS: block design	Proportion of maximum score: 18 for easy and 30 for hard items
Memory and learning	WMS: paired associates	Pairs correct, relative error rates
	Memory for designs	Reproduction accuracy of 10 items: correct (2 points), minor error (1 point)
	Interference recall	Total correct (12 words) and error type
	Similarities recall	Number correct: free and cued recall
	Digit symbol recall	Digit symbol pairs, symbols only, errors

NEUROPSYCHOLOGICAL TASKS

The neuropsychological tasks used were those used in a previous Finnish study of aluminium welders,[3] and they were complemented by a selection of attention and memory tasks. Table 2 shows the neuropsychological tasks classified according to the main cognitive domains assessed, and the summary of measures used.

The simple visual reaction time and finger tapping tasks are subtests from the Swedish performance evaluation system. Embedded figures is a Poppelreuter type of task.[19] In the task used here[20] four sheets, each containing 10 pictures of overlapping objects, were presented. Workers were given one minute a sheet to identify as many objects as possible.

The Santa Ana dexterity test, synonyms, and memory for designs are from the battery of the Finnish Institute of Occupational Health.[21] The synonyms task is a five choice forced recognition test which requires a considerable degree of semantic analysis. Memory for designs is a modification of a visual reproduction task[22] in which the 10 stimuli are designed to make verbal labelling difficult.

The digit-symbol, similarities, and block design subtests from the Wechsler adult intelligence scale (WAIS),[23] and the digit span subtest from the WAIS-R[24] were administered. The present study also incorporated measures of incidental learning for digit symbol and similarities.[19] After completing the digit symbol test, workers drew the correct symbols into the appropriate blank squares below the digits. For the similarities task, both free and cued recall of the items were requested. In the block design task the 10 items were divided according to the degree of preliminary analysis (easy *v* difficult) needed in reconstructing the design.[25] Easy items are those immediately ready for reproduction whereas difficult items need some form of further processing before reproduction.

The materials in the paired associate task were based on the Finnish translation of Wechsler memory scale (WMS)[26] and later modified to include five easy and five difficult pairs.[21] The interference recall task is a homogenous interference task[27] as modified by Kalska (an unpublished method). Workers heard a set of three two syllable words (first set) which they repeated aloud. This was immediately followed by a second set (interference set). After this interference set, workers recalled the first set and then the interference set. Four trials, each consisting of different words, were administered.

The Stroop test used six colours (green, black, red, blue, yellow, and brown) with 84 items in all. The colour naming condition lasted for 40 seconds and the incongruent colour word condition—for example, the word green printed in blue ink—lasted for 80 seconds.

The dual task used is a modification of the task developed by Vilkki.[28] The tasks used were the Bourdon-Wiersma dot cancellation task[21] and a counting backward task. In the dot cancellation task, workers scanned through a series of rows of groups of black dots and had to strike out all groups of four dots for 4 minutes. In the counting task, workers counted backwards in ones from a three digit number for 1 minute. In the dual task condition, tasks were performed concurrently for 2 minutes. A dual task decrement measure, divided attention cost, was computed for both the dot cancellation and counting backwards tasks. This is expressed as the difference between the single and dual task performance divided by the single task performance.[29]

STATISTICAL ANALYSIS

Test scores were analysed with analysis of variance (ANOVA) and analysis of covariance (ANCOVA) controlling for the effects of age or education, Pearson correlations, and multiple linear regression. The only grouping factor was exposure to aluminium (reference *v* low exposure *v* high exposure) and several tasks included additional repeated measures factors. Final testing was performed with the Tukey test and the significance level was set at 5% unless otherwise noted. All reported significance levels are for two tailed tests. All analyses were conducted with SPSS 8.0.[30] Analyses were also conducted controlling for the site at which the testing took place (institute *v* factory), but these did not modify the results.

Results

Table 3 shows the mean performance levels for the neuropsychological tasks in which a single factor ANCOVA was conducted. The only tasks showing potential effects of aluminium groups were the memory for designs

Table 3 Mean (SEM) performance levels in the single factor ANCOVA tasks for the three exposure groups

	Referent (n=28)	Low exposure (n=27)	High exposure (n=24)
Simple reaction time (ms):			
Mean	270 (11)	260 (6)	263 (10)
Standard deviation	46 (3)	50 (3)	50 (5)
Finger tapping:			
Dominant hand	66.79 (1.68)	67.78 (1.58)	67.42 (0.89)
Non-dominant hand	60.64 (1.58)	63.26 (1.69)	60.75 (1.36)
Santa Ana dexterity:			
Dominant hand‡	49.21 (0.89)	47.07 (1.30)	47.33 (1.36)
Non-dominant hand‡	43.39 (1.06)	44.11 (1.21)	42.71 (1.12)
Digit symbol:			
Total correct‡	51.83 (1.66)	47.43 (1.70)	46.15 (1.83)*†
Symbols recalled‡	7.90 (0.23)	7.61 (0.24)	7.31 (0.25)
Pairs correct‡	6.48 (0.409)	6.03 (0.41)	6.63 (0.44)
Omissions‡	0.75 (0.22)	1.34 (0.23)	1.38 (0.25)
Rotation errors	0.36 (0.11)	0.37 (0.11)	0.29 (0.09)
Similarities:			
Total score	18.54 (0.59)	17.96 (0.58)	18.29 (0.53)
Free recall	9.18 (0.61)	9.30 (0.88)	8.63 (0.75)
Cued recall	9.89 (0.25)	9.44 (0.29)	9.42 (0.38)
Synonyms:			
Item selection time (s)§	8.73 (0.51)	8.89 (0.54)	10.46 (0.57)*†
Accuracy (%)	86.60 (2.00)	82.10 (2.10)	80.50 (2.20)
Embedded figures‡	35.02 (0.62)	34.15 (0.63)	33.79 (0.70)†
Memory for designs	18.57 (0.28)	17.22 (0.49)	17.75 (0.30)*

*Significant group effect.
†Significant exposure-response relation.
‡Scores adjusted for age.
§Scores adjusted for education.

$(F(2,76)=3.48, p=0.036)$, digit symbol (total attempted p=0.052) and the forced choice synonyms (item selection time p=0.058) tasks. In the memory for designs task, only the better performance by the reference than the low exposure group (p=0.029) was significant. In the synonym task, education levels were positively correlated with the item selection time $(r=0.293, p=0.01)$. After controlling for this effect, the high exposure group was slower than the low (p=0.050) and reference (p=0.027) groups, but the reference and low exposure groups did not differ. On the digit symbol task, age was negatively correlated with the total items attempted $(r=-0.478, p<0.001)$, and the reference group attempted more than the low (p=0.061) and high (p=0.025) exposure groups. The scores for the low and high exposure groups did not differ.

Table 4 Mean (SEM) scores in the multifactor ANCOVA tasks as a function of exposure groups and the repeated measure factor(s) (scores have been adjusted for the effects of significant covariates)

Task	Reference (n=28)	Low exposure (n=27)	High exposure (n=24)
Block design:			
Easy items	0.942 (0.01)	0.947 (0.02)	0.924 (0.02)
Difficult items	0.798 (0.03)	0.669 (0.03)	0.713 (0.04)*†
Digit span:			
Forward	5.37 (0.20)	5.73 (0.21)	5.88 (0.22)
Backward	4.48 (0.16)	4.43 (0.17)	4.33 (0.18)
Paired associate:			
Easy pairs:			
Trial 1	4.28 (0.18)	4.05 (0.18)	4.08 (0.20)
Trial 2	4.68 (0.11)	4.71 (0.12)	4.66 (0.13)
Trial 3	4.89 (0.07)	4.88 (0.07)	4.89 (0.08)
Difficult pairs:			
Trial 1	1.14 (0.24)	1.62 (0.24)	1.72 (0.26)
Trial 2	2.81 (0.28)	3.17 (0.29)	2.94 (0.31)
Trial 3	3.64 (0.25)	3.70 (0.26)	3.80 (0.28)
Stroop:			
Colour name: total	62.32 (1.79)	60.94 (1.86)	58.64 (2.01)
Colour word: total	33.23 (1.17)	32.14 (1.23)	32.23 (1.31)
Interference recall:			
First set: correct	9.47 (0.40)	8.67 (0.40)	8.66 (0.43)
Interference set: correct	7.70 (0.43)	7.78 (0.44)	7.39 (0.47)

*Significant group effect.
†Significant exposure-response relation.

Pearson correlations were used to explore exposure-response effects. For tasks in which there were no age or education effects, all the simple correlations were insignificant. After controlling for age, urinary aluminium was associated with slower performance in the digit symbol task $(r=-0.241, p=0.035)$ and poorer identification of items in the embedded figures task $(r=-0.219, p=0.055)$. After controlling for education, serum aluminium was associated with slower item selection times $(r=0.256, p=0.027)$ in the synonyms test.

BLOCK DESIGN

A two factor ANOVA, with item difficulty (easy v difficult) as the other factor, showed a borderline effect of groups $(F(2,76)=2.48, p=0.091)$, poorer scores on the difficult items $(F(1,76)=163.3, p<0.001)$, and a group×item difficulty interaction $(F(2,76)=5.63, p=0.005)$. For easy items, the three groups did not differ. For difficult items, the reference group scored higher than the low exposure (p=0.018) group, but no other differences were significant (table 4). The only exposure-response relation showing a significant trend was serum aluminium with difficult items $(r=-0.196, p=0.083)$.

As the embedded figures and memory for design tasks both primarily involve visuospatial processing, this similarity was used to explore block design performance further. Scores on easy items were equally correlated with embedded figures $(r=0.422)$ and memory for design $(r=0.465)$, whereas scores on difficult items were more strongly correlated with memory for designs $(r=0.637)$ than embedded figures $(r=0.437)$. As expected from this pattern, controlling for embedded figures scores left the group×block design difficulty interaction unaltered $(F(2,74)=5.18, p=0.008)$, but controlling for memory for designs scores markedly reduced the significance of the interaction $(F(2,74)=2.76, p=0.070)$. This suggests that the effect on difficult block design items overlaps more with the processes involved in the memory for designs task.

DIGIT SPAN TASK

A two factor ANCOVA, with span type (forward v backward) as the second factor, showed lower spans in older workers (p=0.022), higher forward than backward spans (p<0.001), but no effect of exposure group $(F<1)$ or a span type×exposure group interaction (p=0.127). None of the exposure measures were correlated with performance.

VERBAL PAIRED ASSOCIATES TASK

A three factor ANCOVA on correct recall levels, with pair difficulty (easy v difficult), and trial number (1 v 2 v 3) as the other factors, showed lower recall levels with increasing age $(r=-0.254, p=0.029)$. The usual effects of pair difficulty and trial were present (both p<0.001), and the pair difficulty×trial interaction (p<0.001) simply showed slower learning on the difficult pairs (table 4). However, none of the exposure interactions approached significance (table 4). A similar analysis on the error rates, with pair difficulty and the relative

Table 5 Mean (SEM) scores on the dual task as a function of exposure, task type, and task complexity (work rates have been adjusted for the effects of age)

Task type	Task complexity	Reference (n=28)	Low exposure (n=27)	High exposure (n=23)
Work rate:				
Dots	Single	35.96 (0.96)	36.39 (0.98)	33.95 (1.08)
	Dual	26.38 (1.04)	25.26 (1.07)	22.91 (1.18)†
Counting	Single	54.99 (1.98)	49.82 (2.03)	45.01 (2.23)*†
	Dual	29.24 (1.43)	25.72 (1.47)	22.32 (1.61)*†
Accuracy (%):				
Dots	Single	97.07 (0.63)	96.67 (0.64)	95.15 (0.70)
	Dual	94.63 (1.04)	93.85 (1.06)	94.29 (1.15)
Counting	Single	98.63 (0.84)	98.95 (0.85)	97.30 (0.93)
	Dual	96.83 (0.73)	98.15 (0.74)	96.34 (0.80)
Divided attention costs (%):				
Dots		26.07 (2.18)	30.41 (2.48)	32.42 (3.64)†
Counting		47.07 (2.29)	47.71 (1.93)	50.73 (2.19)

*Significant group effect.
†Significant exposure-response relation.

Effects of exposure to aluminium on work rates in the dot cancellation and backward counting tasks: averaged over single and dual task conditions.

proportion of errors (omission v intrusion from the other list pairs v intrusion from outside the list) as the other factors, simply showed that omissions were the dominant form of error (p<0.001). None of the exposure-response relations approached significance.

STROOP TASK
A two factor ANCOVA, with Stroop condition (colour name v colour word) as the other factor, was conducted on the total number of items named and accuracy. The classic Stroop interference effect was highly significant (p<0.001) for both speed and accuracy (99.6% v 96.8%). Older workers performed the tasks more slowly ($r=-0.393$, p<0.001) and less accurately ($r=-0.267$, p=0.005). The three groups did not differ in work rates ($F<1$), accuracy (p=0.326), and the group×Stroop condition interaction was insignificant for speed ($F<1$), and accuracy (p=0.161). None of the exposure-response relations were significant.

INTERFERENCE RECALL TASK
A two factor ANCOVA, with word set (first set v interference set) as the second factor, was conducted on the total number of words correctly recalled. Education tended to be positively correlated with recall ($r=0.217$, p=0.078) and recall was inferior for the interference set ($F(1,79)=21.8$, p<0.001). However, the group (p=0.525) and the group×word set interaction (p=0.426) were non-significant. Recall errors were classified as failures to recall (omissions), words intruding from one list to another (intrusions between lists) and words not presented (intrusions from outside the lists). Omissions were the most frequent form of error (5.6 v 1.5 v 0.3 respectively; p<0.001), but the exposure (p=0.19) and exposure×error type interaction ($F<1$) were non-significant. None of the exposure-response relation were significant.

DUAL TASK
A three factor ANCOVA, with task type (dot cancellation v backward counting) and task complexity (single task condition v dual task condition) as other factors, was conducted for work rates (items attempted per minute) and accuracy. Work rates were lower in older workers ($r=-0.416$, p < 0.001) and under dual task
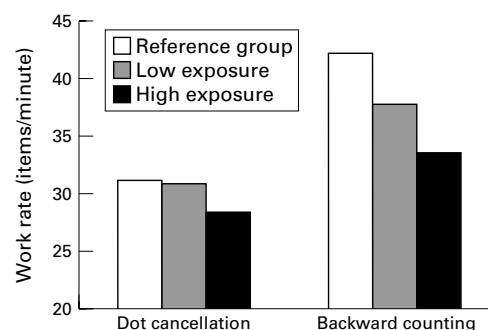
conditions (p<0.001). A significant task type×task complexity interaction (p<0.001) showed that under single task conditions work rates were higher for backward counting (49.94) than dot cancellation (35.43, p<0.01), but under dual task condition the work rates for backward counting (25.76) and dot cancellation (24.85) were identical. There was a main effect of group ($F(2,74)=5.61$, p=0.005) and a group×task type interaction ($F(2,78)=5.33$, p=0.007). Exploration of this interaction (figure) showed that dot cancellation rates were equivalent for the three groups, but backward counting rates were slower in the high exposure group than the reference (p<0.01) group. The low exposure group worked at an intermediate rate, and their scores just failed to differ significantly from the reference and high exposure groups. After controlling for age, backward counting rates were negatively correlated with increasing urinary ($r=-0.275$, p = 0.016) and serum ($r=-0.220$ p=0.055) aluminium. For the dot cancellation task, under single task condition work rates were not correlated with exposure, but under dual task conditions work rates were correlated with both urinary ($r=-0.237$, p=0.038) and serum ($r=-0.236$ p=0.039) aluminium. Accuracy was poorer under dual task conditions (p<0.001) and poorer in the dot cancellation task (p<0.001), but none of the group effects or exposure-response relations were significant (table 5).

For the measures of divided attention cost, although the main effect of exposure was not significant for the dot cancellation task (p=0.251), the exposure-response relations were significant for urinary ($r=0.246$, p=0.030) and serum ($r=0.250$, p=0.027) aluminium. For the backward counting task, the main effect of exposure was non-significant ($F<1$), and none of the exposure correlations were significant.

Given that exposure to aluminium had a clear effect on backward counting, a multiple regression analysis was used to identify tasks that predicted counting rates because this shows information on the functional basis for the effect. The most important factor was the total number correct in the digit symbol task ($\beta=0.338$, p=0.001), followed by total number of items attempted in the Stroop colour naming task ($\beta=0.333$, p=0.001), correct recall of the interference set in the interference memory task ($\beta=0.268$, p=0.002), and backward digit span ($\beta=0.209$, p=0.024). These

four independent influences provided a reasonable prediction of backward counting rates (multiple $R=0.733$, $F(6,67)=16.9$, $p<0.001$; Adjusted $R^2=0.510$) and together indicate that counting backwards is associated with speed when the tasks involve visual scanning and holding information in working memory. However, even after controlling these influences, backward counting rates remained correlated with urinary ($\beta=-0.358$, $p=0.002$) and serum ($\beta=-0.241$, $p=0.044$) aluminium, replicating the pattern obtained after only controlling for age.

Discussion

The aim of the present study was to characterise the cognitive performance profile of MIG welders exposed to aluminium compared with a reference group of mild steel welders. The three exposure groups were about equally sized, with no evidence of concurrent exposure to other neurotoxins, and no current or recent use of antacids containing aluminium. Although the neuropsychological tasks were undertaken at two different sites, controlling for this effect did not modify the findings.

Associations between urinary aluminium concentrations and poorer performance in verbal memory (paired associates and immediate memory span) and immediate visual memory (memory for designs) tasks have been previously found.[3] The results for the verbal memory tasks were not replicated, but similar results for the immediate visual reproduction task were found. Performance on the block design test has sometimes been reported to show impairment with exposure to aluminium[1 2] and sometimes not.[3] In the present study, the distinction between performance on easy and difficult items was examined. The selective effect on difficult items implies that basic visuoperceptual processes are unimpaired and suggests that the processing of the complex visual patterns or the formulation of the plan for reconstructing the spatial arrangement of the blocks is somehow impaired. Results from analysis which partitioned out the influence of performance on two other visuospatial tasks (embedded figures and memory for designs), supports the idea that holding a complex design in memory, and having to reproduce that design, is the basis for the effect on the difficult block design items and is consistent with other data.[2] The block design scoring procedure of allocating extra points for fast correct performance means that the impact of performance speed cannot be disentangled from these conclusions. The incorporation of a recognition memory task would help to determine whether the deficit lies in holding the complex design in memory, or in the formulation and execution of a plan for reconstructing the design.

In the digit symbol task, slower performance was correlated with higher urinary aluminium concentrations. Other studies have reported either impairment[1 2 8] or no impairment.[6] The study reporting no impairment used a computerised version of the task. Although the authors suggest that their test was similar to the traditional task, their version minimises the visual search, learning of symbol digit codes, and motor control components of the task. Changes in test format will change task demands and may lead to differences in sensitivity.

In terms of verbal comprehension, like other studies that used the similarities subtest of the WAIS tests[1–3] no exposure effects were found. On the other verbal task, the synonym test, the high exposure group took longer to make each selection than the low exposure and reference group. Verbal functions are not typically regarded as sensitive to neurotoxins and the exposure-response relations found in the synonym tasks initially seem surprising. However, the similarities test is regarded as more sensitive,[31] most probably due to the verbal reasoning element, and the synonyms test of the present study has a strong reasoning component. No exposure effects were reported in the only other study of aluminium workers' performance in the synonyms task used here,[3] although the performance measure was not specified. However, recent evidence has suggested that verbal abilities may not be as resistant to neurotoxic effects as previously thought.[32] It is suggested that the presence of non-linguistic components (performance speed, visual scanning, and discriminating among several semantically related items in working memory) might underlie the impairment in synonym selection times found here, and perhaps also on other non-hold verbal tests.

Given earlier suggestions that exposure to aluminium impairs attention, two tasks examined attention processes explicitly: the Stroop task and the dual task. The primary theoretical focus in the Stroop task is that of selective attention, and the present study found no evidence that exposure to aluminium influences the ability to inhibit competing information. The second attention related task used was the dual task, which assesses divided attention. Task difficulty, task similarity, and task practice are known to be important in dual task performance and each factor is related to a different theoretical concept.[33 34] Although the dual task used here provided some of the clearest evidence for the effects of exposure to aluminium on cognitive functions, the impairments were not related to the ability to divide attention. Rather, backward counting rates were negatively associated with increasing urinary and serum aluminium concentrations. Before considering the functional locus for this effect, the finding relating to divided attention costs needs to be introduced. The absence of an association between exposure and divided attention costs in the counting task, is consistent with the evidence of an equivalent exposure effect under single and dual task conditions. By contrast, the divided attention costs for the dot cancellation task was positively associated with the urinary and serum aluminium. This finding is also expected given that dot cancellation rates were not correlated with exposure under single task conditions, but were correlated under dual task conditions.

This impairment in dot cancellation divided attention costs could be brought about by two separate mechanisms: a strategy effect or reduced information processing resources. The finding that backward counting rates were higher than dot cancellation rates under single task conditions, but identical under dual task conditions suggests that workers used the strategy of matching (or coupling) their work rates on the two component tasks under dual task conditions. It follows from this that the strategy of coupling work rates under dual task conditions will selectively impair work rates on the dot cancellation task as a function of exposure. The second mechanism relates to reduced processing resources. If the two component tasks draw on the same (visuospatial) resource, this will produce a selective impairment in dot cancellation under dual task conditions. This selective effect can be understood by noting its similarity with backward counting, the two are highly correlated ($r=0.422$, $p<0.001$) in the present study, and the role of visual imagery in backward digit span.[35] In essence, the dual task condition uncovers the effect on dot cancellation due to increased attention demands. Although the strategy explanation seems the simplest, the present data do not allow a choice to be made between the two explanations. To help to differentiate these explanations, it is suggested that studies should more explicitly combine tasks that make demands on the same domain specific resources.

The above explanation is also consistent with factors influencing backward counting rates: speed in tasks involving scanning visually presented material and holding items in memory during concurrent processing. As there is evidence that performance on the trail making B task is related to performance impairments among aluminium workers, whereas trails A is not,[2] those results could also be interpreted as indicating that visual scanning combined with working memory demands constitutes a sensitive indicator of aluminium associated effects.

In general terms, therefore, the present results suggest that aluminium is associated with detrimental effects on certain cognitive functions. What seems common to the tasks showing impairments is the involvement of time limited processing in visuospatial tasks where working memory demands are great. These results, together with the inherent characteristics of the methods used, carry with them several implications for future studies on the cognitive effects of occupational exposure to aluminium and exposure to neurotoxins in general. The current focus in most neurotoxicological research is on low level exposure and consequently the impairments reported are often subtle because they reflect marginal or subclinical changes. The present study suggests that to detect, and more importantly understand, the earliest signs of central nervous system dysfunction it is necessary to apply a theoretically based cognitive approach to the analysis of performance especially for empirically sensitive tasks. The selection of test methods allowing component analysis to be undertaken offer the most likely prospect of showing the elementary cognitive processes underlying impaired performance. The identification of these toxin sensitive processes will allow more explicitly targeted tasks to be devised to explore hypotheses developed to explain the changes in performance. It is only after behavioural data is characterised and interpreted in terms of hypothetical cognitive processes that is it possible for future researchers to select relevant, sensitive, and specific methods. By selecting the appropriate methods, it becomes possible to study further the nature of the impairment found and to provide converging evidence on those cognitive functions that seem to be the most sensitive.

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