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Neurotoxicity of exposures to aluminium welding fumes in the truck trailer construction industry

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Abstract

The aim of the study was to examine aluminium welders for central nervous changes due to the exposure to aluminium containing welding fumes.

A group of 44 aluminium welders in the train body and truck trailer construction industry (mean age: 43 years) with an average of 11.4 years of occupational exposure to aluminium welding fumes and a control group of 37 production workers (mean age: 40 years) of the same plants participated in this longitudinal study. Medical and neuropsychological examinations were performed in 1999 and 2001. Performance was measured with computerised (EURO-NES, motor performance, simple reaction time) and non-computerised test systems (verbal intelligence, standard progressive matrices, trail making, block design) and symptoms with a modified version of the questionnaire Q16. Data was analysed by multivariate analysis of variance including age, education, and alcohol marker as covariates (MANCOVA).

The pre-/postshift average Al-urine concentrations of welders were in the range of 130–153 μg/l. Welders showed significantly poorer performance in symbol-digit substitution, block design, and to some extent in switching attention. However, motor performance and other measures did not differ between welders and controls. Summing up, the results give no clear hints on neurological changes in Al-welders.

Keywords: Aluminium; Welders; Neurotoxicity; Welding fumes; Biomarker; Longitudinal

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1. Introduction

Aluminium (Al) can be found in our environment i.e. in drinking water, food and pharmaceuticals. Occupationally, Al is used in the Al powder and metal industry and in Al foundries. At the working place the inhalative absorption dominates. From the lungs, Al is distributed into the whole organism. It is excreted merely by renal elimination. In occupationally exposed persons Al half-times can vary from days to months, depending on the individual duration of the exposure. Certainly, the bioavailability of different types of Al has to be considered (Letzel et al., 1999).

Al exposure in humans was associated with Alzheimer disease (AD) in the 1990's. However, no conclusive evidence was found that Al contributes to the development of AD (Armstrong et al., 1996; Doll, 1993; Savory et al., 1996).

Epidemiological studies conducted in workers occupationally exposed to Al in various industries, found deficits in some cognitive performance tests. However, the intellectual domain mainly affected varied (Rifat et al., 1990; Hosovki et al., 1990; Sjögren et al., 1990; Hänninen et al., 1994; Akila et al., 1999; Sjögren et al., 1990; Bast-Pettersen et al., 2000; Iregren et al., 2001). Altogether in previous studies on occupational exposure to Al, various changes of different intellectual domains are being discussed.

Bast-Pettersen et al. (2000) found better motor performance in aluminium welders compared to construction workers. However, there were significant relations between tremor

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and years of exposure and between reaction time and aluminium in air.

A recent longitudinal study of Al-welders in the automobile industry, found the motoric movement time of exposed workers prolonged compared to controls (Buchta et al., 2003). However, many other neurobehavioral tests failed to show exposure effects.

The actual study was conducted in a cohort from small and medium size companies. The aim was to examine a higher and longer exposed cohort of Al-welders for neurological changes in dispute.

2. Material and methods

2.1. Study design

This longitudinal study is comprised of three examinations of two cohorts, Al-welders and controls. At the present time, the data from the examinations in 1999 and 2001 can be presented (Fig. 1).

2.2. Cohorts

The two groups comprise employees of five German companies in the train body and truck trailer construction industry. In the first examination, 44 male Al-welders and an age and demographically similar control group of 37 non-exposed production workers of the same plants were included in the study. Thirty-three exposed and 26 non-exposed employees of these cohorts (participation rate: 75% for welders, 70% for controls) were examined again in the second examination. Data of 33 welders and 26 controls could be analysed (Table 1).

Inclusion criteria for welders was a minimum of Al welding of 2 years. Neurological diseases not due to the exposure like cerebrovascular diseases, diabetes, head injuries, as well as insufficient knowledge of the German language and exposure to neurotoxic solvents did lead to exclusion from the cohort. By nationality, 86% of the welders and 92% of the controls were Germans. The exposed employees had a mean exposure to welding fumes of 11.4 years.

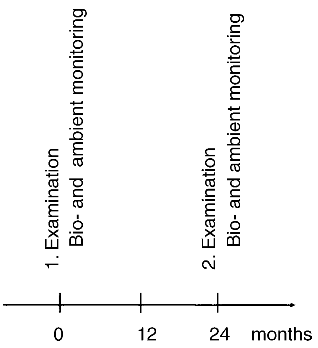

Fig. 1. Design of the longitudinal study on the neurotoxicity of Al-welding fumes.

Table 1
Demographic data of subjects with repeated measurements ($n = 59$)

	Exposed, $n = 33$		Controls, $n = 26$	
	Mean	S.D.	Mean	S.D.
Age (years)	43.3	9.2	39.7	6.6
Education (index)	1.3	0.5	1.2	0.6
CDT (U/l)	5.2	5.9	7.0	10.2
Al-welding (y)	11.4	5.8	–	–

Education index: 0, no elementary school; 1, primary school; 2, secondary school; 3, high school graduation; CDT, carbohydrate-deficient transferrin used as a biomarker for alcohol consumption.

Table 1 shows, that exposed and controls with repeated measurements are largely comparable in age, level of education (four categories: 0–3 and 0, low level), and level of carbohydrate-deficient transferrin in plasma (CDT), which was used as biomarker for alcohol consumption.

The study participants worked either in morning, afternoon or night shift. In order to prevent undue fatigue at the testing in either group, the workers were examined during dayshift between 08:00 and 13:00 h. A precondition was that they had worked on morning or afternoon shift the week before the examination.

2.3. Exposure assessment

We measured individual Al exposure by taking plasma (Al-P) and urinary (Al-U) samples pre and post shift and by personal air sampling for one shift. The monitoring was done close to the day of neurobehavioral testing. Furthermore we applied a questionnaire aimed at documenting the working conditions, working hours, and the individual leisure time exposure. Quantitative determination of Al in plasma and urine samples was carried out by graphite furnace–atomic absorption spectrometry. For calibration, the standard addition technique was used. The determinations were performed under a strict internal and external quality assessment scheme (Lehnert et al., 1999).

2.4. Medical examination

We used a standardised interview focussing on occupational history, education, illnesses, medication, accidents, current alcohol consumption. Furthermore, a physical examination including the neurological status was performed at the testing site.

2.5. Neurobehavioral methods

Neurobehavioral methods were administered to measure possible neurotoxic symptoms, premorbid intelligence, and deficits in the domains of motor performance. The screening was also used to detect differences in logical thinking, short term and working memory, perceptual speed, and switching attention.

We used computerised and non-computerised test systems in our examination. Psychomotor performance tests (Motorische Leistungsserie, MLS), simple reaction time test and European neurobehavioral evaluation system (EURO-NES) were administered computerised.

At examination 2, we introduced EURO-NES and the test of verbal intelligence (WST) for the first time. The rest of the neurobehavioral examinations such as the symptom questionnaire, psychomotor performance test battery, simple reaction time test, recall of digits, block design test, and trail making were performed in examination one and two. The standard progressive matrices test was only applied at examination one, for testing the conformance of the IQ-level of both cohorts.

2.5.1. Verbal intelligence

We applied the German multiple choice vocabulary test (WST, Schmidt and Metzler, 1992) for estimating premorbid intelligence. This test was only used for workers with the German mother tongue.

2.5.2. Q16

The Q16 is a German version of the well-known Swedish questionnaire Q16 (Hogstedt et al., 1984). The questionnaire is a measure for screening workers with psychological and neuropsychological symptoms related to neurotoxic exposure. Three questions were modified and two (related to signs of peripheral neuropathy) were added (Ihrig et al., 2001).

2.5.3. Recall of digits

Recall of digits is part of the German HAWIE. In this short term memory test, the subject had to recall series of digits of increasing length. The maximum achievable points were 14 (2 × 7 series of different lengths) for forward recall as well as for backward recall.

2.5.4. Block design

The block design test is also part of the German HAWIE. The subject had to arrange nine different geometric patterns with 12 cubes with maximum speed. The scores consider the combination of accuracy and speed. A maximum total score of 42 could be achieved.

2.5.5. Psychomotor performance

We used the computerised test battery, with different manual tests, for motor performance (Motorische Leistungsserie, MLS) to measure manual dexterity functions for both cohorts. Psychomotor performances of the upper limbs were screened for by five subtests (‘steadiness’, ‘line tracing’, ‘aiming’, ‘tapping’, ‘peg board’) measuring precision and speed for the dominant and non-dominant hand. The steadiness-test is designed for testing tremor and was administered for 32 s per subject.

2.5.6. Simple reaction time

The task in the test simple reaction time (part of the motor performance test system (MLS)), was for the subject to respond with a quick movement from a home key to a target key whenever a yellow dot appeared on the screen. We recorded reaction time, motoric time, and errors.

2.5.7. Standard progressive matrices

We used a German version (Heller et al., 1988) of the standard progressive matrices test (SPM, Raven) to measure inductive thinking and general intelligence independent of speech. The subject was confronted with the rules of an incomplete matrix of signs and had to fill in the missing sign. The test score indicates the number of correct solutions of 60 matrices.

2.5.8. Trail making test

The German form of the trail making test (TMT; Zahlenverbindungstest, ZVT. Oswald and Roth, 1997) consists of connecting numbers from 1 to 90 in four series. The series are presented on four sheets of paper in different random distributions. Scores represent the average time it takes to complete one series and the mean number of errors.

2.5.9. European neurobehavioral evaluation system (EURO-NES)

Elements from neurobehavioral evaluation system (NES, Letz et al., 1996) and Swedish performance evaluation system (SPES, Iregren et al., 1996) are comprised in EURO-NES (e.g. Gilioli, 1993). The following three tests were administered:

- Symbol-digit substitution
  Perceptual speed, working memory, motor planning and speed are tested. The subject has to perceive a combination of symbols and digits and to complete a new scheme of symbols with the corresponding digits.
- Digit span
  The test is adaptive in difficulty and measures short term memory. It requires the reproduction of digits sequences of increasing length displayed on the screen via keyboard. In the first part, the sequences have to be reproduced forwards, in the second part backwards.
- Switching attention
  The test measures the response speed and the switching of attention towards different features of a complex design. The sign varies in complexity and is displayed on alternating sides of the screen compatible or incompatible to the response keys. The test consists of three parts of increasing difficulty for which reaction time and error measures were collected.

2.6. Statistical analyses

The data was analysed predominantly with descriptive analyses and multivariate analyses of covariance (MAN-

Table 2
Data of biomonitoring in Al-Welders 1999 vs. 2001; Al in urine, urine per creatinine, and plasma

	1999			2001			Wilcoxon/Mann–Whitney	
	Median	Range	*n*	Median	Range	*n*	Paired *p*-value	Independent *p*-value
Respirable dust–air (mg/m^3)	5.6	0–31.5	36	4.5	1.3–15.6	21	.972	.579
Al-U-preshift (μg/l)	136.6	24.8–540.4	33	152.7	2.9–656.3	34	.572	.937
Al-U-postshift (μg/l)	130.0	22.8–810.0	31	145.5	5.0–656.3	25	.445	.760
Al-U-preshift (μg/g creat.)	92.1	17.9–292.2	33	90.1	7.6–420.6	32	.713	.646
Al-U-postshift (μg/g creat.)	97.0	17.9–399.0	31	143.9	8.9–431.8	25	.149	.360
Al-P-preshift (μg/l)	9.6	4.1–31.0	32	10.6	3.3–40.3	34	.122	.624
Al-P-postshift (μg/l)	11.6	5.0–39.6	31	14.3	3.8–51.0	22	.021	.325

COVA) for repeated measurements. The models included Al-exposure (welders versus controls), examination (two measurements, repetition factor) and the covariates age, education and CDT. Applying a repeated measurements model offered the possibility of additionally testing the hypothesis whether exposed and controls changed differently from examination 1 to examination 2 (interaction term: exposure × examination). Changes of exposures were checked with nonparametric two-sample tests.

3. Results

3.1. Biomonitoring and ambient monitoring

Several parameters of Al-concentration in plasma and urine in welders increased from examination 1 to examination 2 (Table 2). Plasma levels increased from 9.6 μg/l (1999) to 10.6 μg/l (2001, Al-P-preshift) and from 11.6 μg/l to 14.3 μg/l (2001, Al-P-postshift). Six wokers exceeded the

Table 3
Means and standard deviations of motor performance tests (dominant and non-dominant hand), simple reaction time, and symptom questionnaire Q16 for exposed and non-exposed workers 1999 vs. 2001 (sample with repeated measurements)

		Exposed 1999, *n* = 33		Exposed 2001, *n* = 33		Non-exposed 1999, *n* = 26		Non-exposed 2001, *n* = 26	
		Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Motor performance									
Steadiness									
Errors (*n*)	dom. hand	9.2	17.6	1.8	2.8	9.4	13.0	1.8	3.0
Error time (ms)	dom. hand	0.5	1.1	0.1	0.2	1.0	2.8	0.1	0.2
Line tracing									
Errors (*n*)	dom. hand	22.7	9.5	21.3	10.2	22.1	7.1	21.3	7.0
Error time (ms)	dom. hand	2.0	1.1	2.0	1.2	1.9	0.8	1.7	0.6
Aiming									
Hits (*n*)	dom. hand	19.9	0.5	19.7	0.5	19.8	0.5	19.8	0.7
Total time (ms)	dom. hand	7.1	1.4	7.3	1.4	7.1	1.2	7.2	1.2
Tapping									
Hits (*n*)	dom. hand	201.2	20.5	197.4	22.5	197.2	43.3	199.6	17.8
Steadiness									
Errors (*n*)	nd. hand	11.2	15.8	2.4	3.3	12.1	11.8	2.7	2.6
Error time (ms)	nd. hand	0.8	1.1	0.2	0.2	0.9	1.3	0.2	2.2
Line tracing									
Errors (*n*)	nd. hand	28.7	10.9	28.1	9.6	27.1	11.3	24.8	7.9
Error time (ms)	nd. hand	2.7	1.5	2.7	1.1	2.7	0.9	2.5	1.0
Aiming									
Hits (*n*)	nd. hand	19.0	3.7	19.1	5.0	20.2	0.8	19.9	0.6
Total time (ms)	nd. hand	7.7	1.4	8.2	1.5	7.6	1.2	7.9	1.5
Tapping									
Hits (*n*)	nd. hand	183.9	20.5	178.2	19.3	182.9	23.7	183.2	21.2
Simple reaction									
Reaction t.(ms)		274.4	46.4	271.7	46.3	269.9	52.5	275.9	47.0
Movement t.(ms)		171.7	40.7	159.8	41.1	153.2	45.9	159.9	53.7
Q16 sum (*n*)		2.7	2.3	2.5	2.5	1.8	1.8	1.5	1.4

German BAT-Value for urinary Al of 200 µg/l. In contrast, respirable dust exposure decreased from a median 5.6 mg/m^3 to 4.5 mg/m^3. The differences in dust and biomonitoring measures between 1999 and 2001 were tested with nonparametric methods. The Wilcoxon test for matched pairs indicated a significant increase of aluminium in plasma postshift ($p = .021$). However, the Mann–Whitney *U*-test for two independent samples, considering all available measurements for each variable, indicated no significant differences.

3.2. Q 16 symptoms

The mean number of reported neurobehavioral symptoms decreased slightly from 2.7 (1999) to 2.5 (2001) symptoms in exposed and from 1.8 (1999) symptoms to 1.5 (2001) in controls (Table 3). No significant difference between both cohorts could be observed (Table 4) concerning Q16 symptoms. A detailed analysis of the number of subjects reporting more than a critical level of five symptoms did not reveal significant differences between welders and controls.

3.3. Psychomotor performance

The data of the motor performance testing are presented in Table 3 for the dominant and non-dominant hand. The differences between exposed and controls are small. For each performance task, the speed data were analysed together with the accuracy data for both hands in one model by multivariate analysis of covariance (MANCOVA) for repeated measurements with age, education and CDT as covariates (Table 4). No significant differences were detected between cohorts for steadiness, line tracing, aiming, or tapping.

From examination 1 to examination 2, we generally found small improvements in all variables of psychomotor performance. The improvement in steadiness may be due to an unknown change in the system or procedure. There is no significant difference in change in performance between exposed and controls from examination 1 to examination 2 (interaction term: examination × exposure).

3.4. Simple reaction time

The multivariate analysis of covariance in the simple reaction time task included reaction time (decision time) and motoric movement time in one model. Exposed and controls did not differ significantly in their results of examinations 1 and 2 or their trends from one examination to the other, whereas the factor age was significant (Tables 3 and 4, Fig. 2). The interaction examination × exposure is marginally nonsignificant ($p = .053$, Table 4). However, in contrast to a neurotoxicological deterioration, the performance in welders improved from the first examination to the second (Fig. 2).

Table 4
Results of multivariate and univariate analyses of covariance for repeated measures of motor performance, simple reaction, and symptoms (Q16)

		Exposure			Age			Education			CDT			Examination			Examination × exposure		
		F	*p*	η^2	*F*	*p*	η^2	*F*	*p*	η^2	*F*	*P*	η^2	*F*	*p*	η^2	*F*	*p*	η^2
Steadiness																			
Errors (*n*)	dom. hand	.370	.829	.028	.663	.621	.049	.875	.486	.064	.401	.807	.030	.071	.991	.006	.258	.904	.020
	nd. hand																		
Error time (ms)	dom. hand																		
	nd. hand																		
Line tracing																			
Errors (*n*)	dom. hand	2.039	.103	.138	3.087	.024	.195	1.016	.408	.074	.375	.825	.029	.400	.808	.030	.831	.512	.061
	nd. hand																		
Error time (ms)	dom. hand																		
	nd. hand																		
Aiming																			
Hits (*n*)	dom. hand	.831	.512	.061	2.832	.034	.182	.546	.703	.041	.326	.859	.025	.208	.933	.016	.593	.669	.044
	nd. hand																		
Total time (ms)	dom. hand																		
	nd. hand																		
Tapping																			
Hits (*n*)	dom. hand	.284	.754	.011	.593	.556	.022	.141	.869	.005	.003	.997	.000	.377	.688	.014	1.158	.322	.042
	nd. hand																		
Simple reaction																			
Reaction time (ms)	dom. hand	.177	.838	.007	3.856	.027	.127	.271	.764	.010	1.580	.215	.056	2.209	.120	.077	3.105	.053	.105
	nd. hand																		
Movement time (ms)	dom. hand																		
	nd. hand																		
Q16		2.411	.126	.041	7.166	.010	.113	2.701	.106	.046	.001	.972	.000	5.068	.028	.083	.257	.614	.005

Exposure and examination are grouping and repetition factors, respectively. Age, education, and carbohydrate-deficient transferrin (CDT) are covariates. *F*, *F*-value; *p*, *p*-value; η^2, portion of explained variance.

Table 5
Means and standard deviations of cognitive performance tests

	Exposed 1999		Exposed 2001		Non-exposed 1999		Non-exposed 2001	
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.
Cognitive performance								
HAWIE								
n	32		32		26		26	
Digit span								
Forward (*n*)	6.6	2.1	8.9	2.5	7.9	2.6	10.3	2.4
Backward (*n*)	5.7	1.8	8.2	1.9	6.4	1.6	8.9	2.5
Block design	25.2	6.4	31.2	4.3	30.6	6.6	34.6	5.3
Trail making								
Errors (*n*)	2.9	3.0	0.9	4.3	2.6	1.9	0.0	0.0
Time (ms)	89.6	25.8	83.1	32.9	81.5	31.0	75.6	33.3
n	44				37			
S.P. matrices	44.2	7.9			47.4	7.5		
n			23				17	
Verbal IQ			96.4	6.5			98.8	5.8
EURONES								
n			30				18/2	
SDS (ms)			3286.7	640.7			2646.8	522.5
Digit span								
Forward (*n*)			5.4	0.9			6.1	1.0
Backward (*n*)			4.0	2.1			4.9	2.2
Switching att.								
Reaction time (ms)								
Side			414.0	72.4			370.0	64.8
Arrow			793.8	247.1			607.7	135.1
Mixed			783.8	249.2			608.7	213.9
Errors (*n*)								
Side			.5	.7			.2	.7
Arrow			2.1	3.7			.5	.7
Mixed			6.6	7.1			2.4	3.2

F, *F*-value; *p*, *p*-value; η^2, portion of explained variance.

3.5. Cognitive performance

3.5.1. Non-computerized tests

For estimating the verbal IQ, we applied a multiple choice vocabulary test (WST) in the subgroups of exposed and control subjects with German native language in the second examination. However, these subgroups did not differ significantly (Table 6) and revealed an average IQ of 96.4 for welders and 98.8 for controls (Table 5). We used education as a covariate to control for intellectual differences, as it was not possible to implement vocabulary results as a covariate for the total group.

The standard progressive matrices test (SPM), a test of logical reasoning and general intelligence, was performed in the first examination with the total samples of exposed and control subjects and led to a small nonsignificant difference (mean exposed: 44; mean controls: 47) in the mean values (Tables 5 and 6).

The trail making performance was analysed multivariately to control the possible trade off effects between accuracy (errors) and speed (time). The performance increased nonsignificantly from examination one to two. Trail making showed a clear influence of age ($p = .003$; $\eta^2 = 0.202$), but no influence of exposure or CDT (Table 6).

Block design (HAWIE), like SPM a measure of so-called fluid intelligence, revealed a higher performance level of non-exposed compared to exposed ($p = .01$, $\eta^2 = 0.12$, Table 6). Also age was highly significant ($p = .000$, $\eta^2 = 0.29$) but not the interaction examination × exposure.

Digit span was studied in verbal (HAWIE) and computerized (EURO-NES, only examination two) form. The MANCOVA model of the verbal task included repeated measurements of forward and backward performance. There were no significant exposure or exposure interaction effects (Table 6).

3.5.2. Computerized tests: EURO-NES

The EURO-NES test was introduced in 2001 with examination 2 the first time. In the last examination in 2003, it will be repeated. The subtest digit span in EURO-NES is a way to investigate the maximal short term memory performance of a subject. In our cohort exposed workers could remember

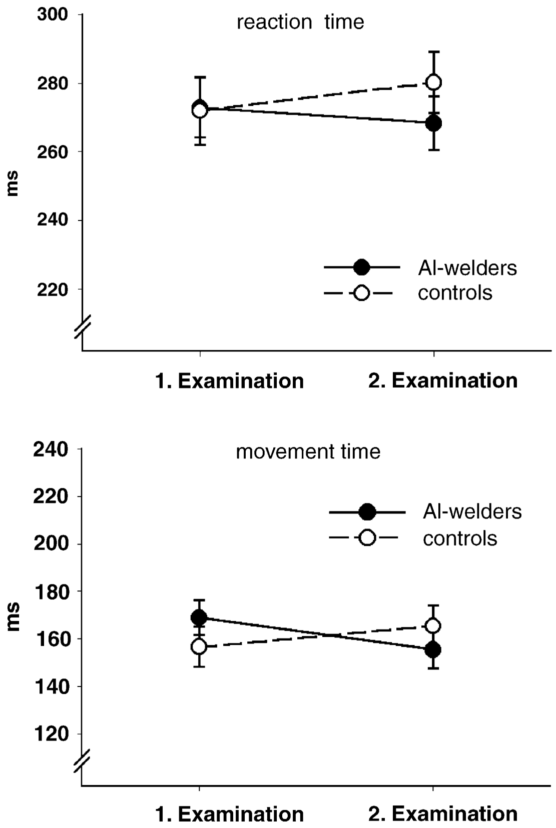

Fig. 2. Reaction time and movement time (simple reaction test) adjusted for education, age, and alcohol consume (CDT) of Al-welders and controls. The interval between examinations is 2 years.

on average 5.4 numbers forward and 4.0 numbers backward whereas controls could remember on average 6.1 numbers forward and 4.9 numbers backward (Table 5).

A strong working memory component is part of the subtest symbol-digit substitution. Thus, symbol-digit substitution and digit span forward and backward were analysed together by multivariate analysis. Al-welders showed a significantly lower performance ($p = .043$, Table 6). Age explained a significant and substantial part of variance, 22% and CDT, 9% (Table 6). Fig. 3 demonstrates that welders revealed worse performance in the symbol-digit substitution SDS test (Fig. 3, SDS univariate: $p = .012$).

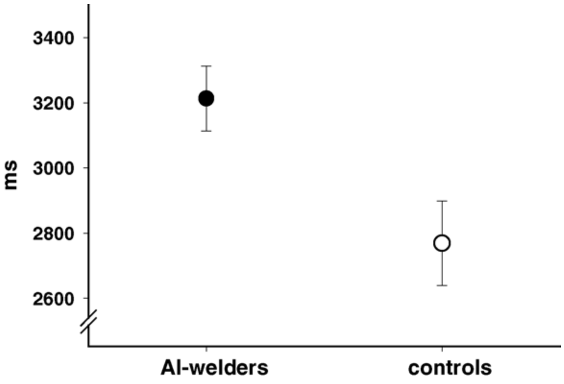

Fig. 3. Symbol-digit substitution (SDS) performance at examination 2 adjusted for education, age, and alcohol consume (CDT) of Al-welders and controls..

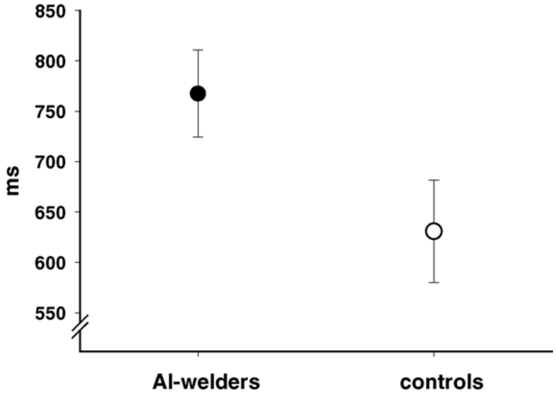

Fig. 4. Switching attention (arrow, EURO-NES) performance at examination 2 adjusted for education, age, and alcohol consume (CDT) of Al-welders and controls.

In the EURO-NES, the switching attention subtests were analysed multivariately for the three parts of the test (side, arrows, mixed) including both reaction time and errors. We found nonsignificantly lower performance levels in Al-welders compared to controls.

However, univariate covariance analysis revealed significantly poorer performance of welders in the arrow-part of the switching attention test (d.f. = 1, $F = 6.012$, $p = .018$, $\eta^2 = .113$, Fig. 4) and marginally nonsignificant results for the mixed part.

4. Discussion

The results in the neurobehavioral field of this, and other studies suggest that the used performance measures, e.g. of the computer tests, are sensitive to age (Kiesswetter et al., 2000; Letz et al., 2003). The studies reveal a significant performance decline in neurobehavioral measures caused by biological ageing. Therefore, a corresponding sensitivity of these measures to neurobehavioral changes caused by neurotoxic exposures should be expected, especially if high and long-lasting neurotoxic exposure can be assumed.

The median urinary Al-concentrations of the welders in our study were in 1999 and 2001 in the range of 130–153 μg/l which is much higher than the levels reported by other studies on Al-welders (Sjögren et al., 1990; Hänninen et al., 1994; Akila et al., 1999; Bast-Pettersen et al., 2000; Iregren et al., 2001; Buchta et al., 2003). The exposed workers in our study had welded over 11.4 years. In previous studies, the range of urinary Al-concentration was 22–65 μg/l and the average exposure time 4–15 years. The number of studied subjects varied between 20 and 28 (Bast-Pettersen et al., 2000; Iregren

Table 6
Results of multivariate and univariate analyses of covariance for repeated measures of cognitive performances

		Exposure			Age			Education			CDT			Examination			Examination × exposure		
		F	*p*	η^2	*F*	*p*	η^2	*F*	*p*	η^2	*F*	*p*	η^2	*F*	*p*	η^2	*F*	*p*	η^2
HAWIE																			
Digit span																			
Forward (*n*)		1.718	.189	.062	.020	.981	.001	3.080	.054	.106	2.990	.059	.103	3.886	.027	.130	.031	.969	.001
Backward (*n*)																			
Block design		7.116	.010	.118	21.851	.000	.292	.044	.835	.001	.105	.747	.002	.023	.881	.000	2.032	.160	.037
Trail making																			
Errors (*n*)		.638	.532	.024	6.591	.003	.202	.185	.832	.007	.545	.583	.021	.103	.902	.004	.331	.720	.013
Time (ms)																			
Verbal IQ	(exam. 2)	1.476	.23	.037	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
S.P. matrices	(exam. 1)	1.093	.299	.014	25.094	.000	.248	2.131	.148	.027	.343	.560	.004	–	–	–	–	–	–
EURONES																			
SDS (ms)	(exam. 2)	2.968	.043	.178	3.946	.015	.224	1.402	.256	.093	1.292	.290	.086	–	–	–	–	–	–
Digit span																			
Forward (*n*)																			
Backward (*n*)																			
Switching attention	(exam. 2)																		
Reaction time (ms)																			
Side																			
Arrows																			
Mixed																			
Errors (*n*)	1.372	.248	.164	1.957	.094	.218	1.579	.177	.184	.260	.952	.036	–	–	–	–	–	–	–
Side																			
Arrows																			
Mixed																			

Exposure and examination are grouping and repetition factor, respectively. Age, education, and carbohydrate-deficient transferrin (CDT) are covariates. *F*, *F*-value; *p*, *p*-value; η^2, portion of explained variance.

et al., 2001; Hänninen et al., 1994; Sjögren et al., 1990). Altogether, the exposure time and the urinary Al levels in our study were higher than in the cited studies.

Motor performance was the main neurobehavioral domain affected in the above mentioned comparable studies. With the same methods as applied here, the variable simple reaction time was significantly affected in our study in the automobile industry (Buchta et al., 2003).

Exposure to aluminium in the present study was relatively pure, while exposures in other studies also included solvents, manganese and other welding fumes. However, in this study, the effect on simple reaction time, found with pure Al exposure in our "automobile study" (Buchta et al., 2003), could not be replicated. It might be an accidental effect related to the error probability of 5%. In the present study, we found significant differences between welders and controls ín a EURONES multivariate outcome (symbol-digit substitution + digit span forward/backward) and block design (HAWIE). In the present study, welders had a lower performance level in block design in both examinations, but no trend differences compared to controls were detected. Comparable results were not observed in the automobile study. However, in both studies, the questionnaire Q16 gave no suggestion of neurobehavioral disorders.

Both studies, although using the same methods, result in statistical significant effects in different performance areas. Comparing the performance trends of welders and controls in the actual data, where repeated measurements were available, no adverse exposure related developments could be detected. Therefore, the observed significant effects in examination 2 of the present study may be based on a priori group differences not depending on aluminium exposure.

The existing heterogeneous results do not allow a clear deduction of exposure effects. A third examination will provide the opportunity to perform additional trend analysis to either support or defeat the hypothesis of exposure related effects. To ascertain exposure effects, the neurobehavioral performance trends of welders and controls should persistently diverge. To detect these effects, a longer time period may be needed. The actual examination may not have been long enough to observe the existence of exposure effects. However, as the sample size available for those tested on both occasions was rather small, the power to detect significant effects is limited. Also, the possibility of a "healthy worker effect" has to be considered, since the average exposure time was >11 years and the inclusion criteria was a minimum exposure of >2 years. Some individuals, who have experienced symptoms, might have left the plants.

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