

Neuropsychological function among workers exposed to aluminum – a mini-review

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Abstract: Aluminum (Al) is the most common element in nature after oxygen and silicon. Aluminum has been proposed to be a causative agent in the development of neurodegenerative diseases. Aluminum made available via the lungs, as it is in occupational settings, is probably better absorbed than that entering the body via the gastrointestinal tract. Neuropsychological tests are sensitive methods for detecting subtle functional impairment of the nervous system. This minireview is based on a systematic literature search for studies on workers occupationally exposed to aluminum. The tests were categorized as belonging to one of 12 different neuropsychological functions. The level of significance was set at $p < 0.05$. Among the 559 papers identified, 24 fulfilled the inclusion criteria. There were no clear, consistent findings of occupational aluminum exposure being correlated with neuropsychological deficits. However, there was a weak tendency toward worse performances on tests related to information processing speed and a slight tendency toward weaker performances on memory tests for workers exposed to aluminum. The limited number of studies in this field makes it difficult to draw a clear conclusion regarding whether occupational exposure to aluminum increases the risk of altered neuropsychological function.

Key words: Aluminum production, Aluminum welders, Neuropsychological tests, Speed of information processing, Memory

Introduction

Aluminum (Al) is the third most common element in nature after oxygen and silicon, representing approximately 8% of the Earth's crust by weight. Aluminum is a light metal with a specific gravity of 2.7, and although it is not found in its metallic form in nature, its compounds are present in almost all rocks, soils, and clays.

Aluminum is used in aircraft, train, and car construction

as well as in building materials, electrical conductors, kitchen utensils, and packaging. This metal is not known to serve any essential biological functions in the human body. In the body, aluminum mainly accumulates in the bone (50%), lungs (25%), kidney and liver¹). The brain has a lower aluminum concentration than many other tissues, and aluminum enters the brain primarily through the blood-brain barrier²). The molecular processes that are linked with aluminum transport are still unclear. It is suggested that aluminum competes with iron to bind with iron transporters (transferrin), which are also involved with aluminum transport via the blood-brain barrier³).

For persons not occupationally exposed, the most important sources of aluminum intake are food and drinking

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water. Aluminum in drinking water accounts for only a fraction of the amount taken in via food and drink, probably approximately 1%⁴) but possibly as much as 2.2%⁵). Important sources of aluminum in food include infant formulas, baking powder, bakery mixes, dried vegetables and food additives. The aluminum content is generally lower in fresh meat and fish and higher in vegetables, grains, and spices²). Other sources of intake are medicinal products containing aluminum (especially antacids) and cosmetic products¹). The presence of food in the stomach generally reduces/inhibits aluminum absorption, but the presence of citrate (for example, from orange juice) enhances aluminum absorption¹). The daily median aluminum intake is less than 10 mg, and more than 95% of excretion occurs in the urine²).

In 1976, dialysis encephalopathy syndrome was first described in a group of dialysis patients who experienced serious neurological disturbances⁶). The dialysis fluid contained aluminum, meaning that these patients with kidney disease were both heavily exposed to aluminum and essentially unable to excrete it.

A question was raised regarding whether aluminum causes or contributes to the development of neurodegenerative diseases, mainly Alzheimer's disease. This disease causes a distinct pattern of pathological changes in the brain, among which abnormal accumulations of tau protein, neurofibrillary tangles (NFTs) inside neurons, and beta-amyloid plaques outside and around nerve cells are the most prominent⁷).

The central question was whether aluminum contributes to the development of Alzheimer's disease or whether elevated aluminum concentrations in Alzheimer's patients are a consequence of the disease—for example, previously existing disturbances in the blood-brain barrier may allow the passage of more aluminum, and NFTs and beta-amyloid plaques may bind aluminum⁴). Later, the hypothesized similarity between aluminum-induced dialysis encephalopathy and Alzheimer's disease could not be confirmed. Dialysis encephalopathy was shown to be caused by aluminum, but it results in a different neuropathology⁴).

The description of the dialysis encephalopathy syndrome contributed to the question of whether subjects occupationally exposed to aluminum have an increased risk of impaired nervous system function. Aluminum made available via the lungs, as in occupational settings, is probably better absorbed than that entering the body via the gastrointestinal tract^{1,5}). Studies have shown elevated concentrations of aluminum in the serum and urine of aluminum-exposed workers⁸), confirming that aluminum is absorbed.

Another question raised was whether aluminum in drinking water increases the risk of dementing illnesses, including Alzheimer's disease²), but this question is beyond the scope of the present study.

Clinical neuropsychology is an applied science concerning behavioral expression in cases of brain function/dysfunction⁹). While severe nervous system disturbances can be observed clinically, the anticipated small effects of exposure to low levels of neurotoxicants cannot. Neuropsychological tests are sensitive methods that are often used to detect subtle functional impairments of the nervous system⁹). Such test methods can be used to systematically assess cognitive functions in large groups, providing measures that can be treated and analyzed statistically. While most neuropsychological tests focus on cognitive functions, assessments of speed and motor functions are also included in neuropsychological test batteries.

The minireview aimed to present and analyze existing knowledge obtained from international research on work-related exposure to aluminum and its possible effects on neuropsychological functions.

Material and Methods

Search strategy and inclusion criteria

A systematic literature search was performed using PubMed with the assistance of the Biomedical Library, University of Gothenburg. The search was completed in December 2018 and was restricted to studies published in English. The search string included the exposure term aluminum/aluminium, outcome terms related to neuropsychological functions, and terms for different neuropsychological tests and was restricted to studies on occupationally exposed adults. Only studies fulfilling a specific criteria set were included for further examination.

The inclusion criteria were studies with N>10 participants in which neuropsychological test methods were applied. The studies further had to include either a control or comparison group or a differentiation in terms of levels of exposure or comparison with established norms. Only studies involving at least one test that could be classified as neuropsychological were included. The Mini Mental State Examination (MMSE)¹⁰) and the Clock Drawing Test¹¹) are simple tests that meet the minimum requirements for being neuropsychological. Neurological studies alone were not included, but some tests assessing motor functions such as tremor and grip strength, which border between neuropsychology and neurology, were included. Studies on subjects involved in litigation processes were not included.

All tests applied in the included studies were evaluated and categorized as belonging to one of 12 different neuropsychological functions, and a simplified scoring system was used. Test results for certain functions indicating statistically significant impaired performance in the exposed group were categorized as differences between exposed and referents for these functions and denoted with a “+”. Because the scoring system did not allow for more than one “+” for each function, several tests covering the same function and indicating significant impairment could not be scored higher than one “+”. Similarly, differences in the range of p-values between ($p > 0.05$ and < 0.10) were denoted as “(+/-)”. If none of the tests applied for that specific function showed worse performance, the score was “-”. If no tests were available for a specific function, no score was given for that function. Regarding the overall trends, a sum score was calculated for each function by assigning 1 to the “+”, 0.5 to the “(+/-)”, and 0 to the “-” and then dividing the scores by the total number of scores for each function. The applied level of significance was set at $p < 0.05$.

Neuropsychological functions

A 1983 meeting of an expert group resulted in a screening battery of seven “core tests” for detecting neurotoxic effects in humans. The test battery was named the World Health Organization Neurobehavioral Core Test Battery (WHO NCTB)¹². Over the years, a wider range of neuropsychological tests has been applied in the neurotoxicology field to study the possible effects of occupational exposure on neuropsychological functions. Most of the tests are described in the compendiums by Lezak *et al.*⁹ and Strauss *et al.*¹³; hence, for these tests, no individual references are provided. In the following, the relevant functions are described in the same order as they are presented in the table describing the outcomes of exposure.

Studies with low exposure and anticipated small effects are liable to be affected by the presence of confounding factors associated with both the studied exposure and the outcome. Neuropsychological test results vary with increasing age, the level of education and gender¹⁴. When comparing performances on tests for cognitive function, the groups under study should ideally be as identical as possible in all aspects other than the exposure. Adjustment for the “pre-exposure” intellectual level is generally based on the years of formal education or on tests that are assumed to measure general intellectual ability¹³. There are diverse conceptions of general cognitive capacity and intelligence and how these features can be measured. Among other factors, intelligence comprises the global capacity of

a person to act purposefully, think rationally, and deal effectively with his or her environment¹⁵. The Wechsler Adult Intelligence Scale (WAIS; the WISC for children) is often considered the gold standard for the assessment of general cognitive capacity and intelligence¹³.

Verbal academic skills/verbal comprehension is a central element of a person’s general intelligence and is a central factor/element of the General Ability Index (GAI)¹⁵. When calculating IQ via the WAIS, the “Verbal Comprehension Index” accounts for 30% of the full-scale IQ. Tests regarded as covering verbal comprehension in the WAIS include Similarities, Vocabulary, Information, and Comprehension. Other tests not in the WAIS battery are the Aphasia Screening Test and Boston Naming Test.

Spatial skills/perceptual organization or perceptual reasoning is another central factor of a person’s general intelligence and covers nonverbal abstract problem solving, visual spatial reasoning, and the ability to quickly perceive visual details. In the WAIS, the “Perceptual Reasoning Index” accounts for 30% of the full-scale IQ. Tests that are regarded as covering spatial skills/perceptual organization or perceptual reasoning in the WAIS include Block Design, Matrix Reasoning, Visual Puzzles, Picture Completion, and Figure Weights. Other tests not in the WAIS battery are the Tactual Performance Test-Time and Raven’s Progressive Matrices.

Speed of information processing/processing speed can be defined as the ability to perform simple, repetitive cognitive tasks quickly and fluently¹⁶; in other words, processing speed is the time it takes a person to perform a mental task. In the WAIS, the “Processing Speed Index” accounts for 20% of the full-scale IQ, but this index is not included when calculating the GAI. Tests that cover processing speed/perceptual organization or perceptual reasoning in the WAIS include Digit Symbol/Coding, Symbol Search, and Cancellation. Other tests not in the WAIS battery are the Trail Making Test A, Stroop Words, Stroop Color, Color Trails 1, and Symbol Digit Modalities Test (SDMT).

Attention/working memory, previously called short-term or immediate memory, refers to the ability to store information for a very short time, usually from a few seconds to several minutes. As working memory is not dependent on storing the information, it is usually classified as an element of attention. In the WAIS, the “Working Memory Index” accounts for 20% of the full-scale IQ, but this index is not included when calculating the GAI. Tests for attention/working memory in the WAIS include Digit Span, Arithmetic, and Letter-Number-Sequencing. Other tests not in the WAIS battery are the Paced Auditory Serial Addition

Test (PASAT), Seashore Rhythm Test, Speech Sounds Perception Test, and CANTAB Spatial Working Memory test.

Long-term memory is often divided into two major parts: explicit (conscious or declarative) and implicit (unconscious, nondeclarative or procedural). Implicit memory refers to a heterogeneous collection of abilities (skill learning or procedural memory), such as how to swim and ride a bicycle.

Explicit memory can be divided into episodic and semantic memory. While episodic memory stores personal, autobiographical memories, semantic memory stores factual information, such as the capital cities in a geographic region. Most tests of long-term memory are on explicit memory because this is the most realistic approach in a structured test setting. Tests for *verbal memory* include the Verbal Paired Associates task, word list learning tasks such as the California Verbal Learning Test (CVLT), the Rey Auditory Verbal Learning Test (RAVL; 10, 12 or 15 words), and story memory/logical memory tasks. Tests for *visual memory* include the Visual Paired Associates task, the Benton Visual Retention Test, the Rey-Osterreich complex figure test, and the Memory for Faces test (Warrington).

Executive functions refer to a complex set of processes that have been broadly and variously defined¹³. Lezak *et al.*⁹ describe executive functions as capacities that enable a person “to engage successfully in independent, purposive, self-directed, and self-serving behavior”. The central aspects of executive function are volition, planning, purposive action, and effective performance¹³. Tests regarded as covering executive functions include the Wisconsin Card Sorting Test, Trail Making Test B, Color Trails 2, Stroop Test (color-word interference), Halstead Category Test, and Letter Fluency FAS.

Reaction time/response speed can serve as a relatively direct way to assess processing speed. Simple reaction time is frequently slowed with brain disease or injury, and reaction time differences between healthy and demented subjects become much larger when stimuli choices and/or response choices are introduced⁹. Tests for reaction time include the Neurobehavioral Evaluation System (NES 2&3)¹⁷ and the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Tests of *manual dexterity/manual speed* have frequently been included in neuropsychological examinations. Brain disorders often, but not always, have a slowing effect on the finger tapping rate, and evidence exists that peg-placing speed is reduced by a number of conditions, including toxic exposure¹³. Tests of manual dexterity/manual speed include the Grooved Pegboard Test, Purdue Pegboard Test,

and Finger Tapping Test/Finger Oscillation Test.

Tremor is defined as “any involuntary, approximately rhythmic, and roughly sinusoidal movement of a body part”. It is produced by alternating or synchronous contractions of antagonist muscles. Tremor is characterized by its frequency (Hz) and amplitude, and exposure to several neurotoxins has been reported to cause tremor¹⁸. Tremor can be tested via the CATSYS Tremor Pen, Nine-hole Steadiness/Static Steadiness Test, and Motor Steadiness test.

Other motor skills refer to a variety of functions, among which grip strength is measured in several neuropsychological studies. There is evidence that changes in grip strength correlate moderately with changes in cognitive functioning¹³. Among the tests categorized as “other motor skills” are hand dynamometers to test grip strength, eurythmokinometers (EKMs) and pursuit aiming.

Symptoms/subjective complaints can be an early indication of encephalopathy. Symptom questionnaires are commonly used to monitor workers who are occupationally or environmentally exposed to neurotoxicants, shift work, bullying, etc¹⁹. The following questionnaires are often used in occupational health settings: The Profile of Mood Scale (POMS), the Q16, and the Euroquest.

Results

Altogether, 559 papers were identified from the literature search, and 24 studies were found to fulfil the inclusion criteria and were subsequently included in the study. Eleven studies were on workers in aluminum production plants^{20–30}, and ten were on aluminum welders^{31–40}. One study comprised workers with different kinds of exposure⁴¹, one study was comprised of workers who recycled aluminum in a salvage plant⁴² and one study examined workers who inhaled aluminum powder⁴³.

In Table 1, the studies are presented in chronological order by publication date. The table reports the study results in 12 different neuropsychological domains. Among the 24 studies, approximately 1800 exposed subjects were included, but this number depended on whether workers with low exposure were regarded as exposed individuals or as referents. Two studies covering 286 subjects gave no indication of exposure other than years exposed^{21, 43}.

The first study⁴³ which assessed underground miners who inhaled aluminum dust (“McIntyre Powder”) to protect themselves from the pulmonary disease silicosis, had a large impact on subsequent research in this field. Overall, 261 underground miners and 346 referents were examined

Table 1. Neuropsychological function in workers exposed to aluminum

Epidemiological studies of workers exposed to aluminum	N Exposed/Referents	Type of exposure characterization	Years exposed	Verbal/academic skills	Spatial skills/perceptual organization	Speed information processing	Attention/working memory	Verbal memory	Visual memory	Executive functions	Reaction time	Manual dexterity/speed	Tremor	Other Motor skills	Symptoms
Rifat <i>et al.</i> ⁴³⁾	261 /346	Y; -	>20/10-20/ <10	-	+	+	-	-	-	-	-	-	-	-	-
Hosovski <i>et al.</i> ²⁰⁾	87/60	Y; A; B; U	18.9	-	+	+	+	-	-	-	+	-	-	-	-
White <i>et al.</i> ²¹⁾ a	25/-	Y; -	18.7	-	-	-	-	+	+	-	-	-	-	-	+
Bast-Pettersen <i>et al.</i> ²²⁾	22/ 16	Y; A; S; U	19.2/19.6	-	(+/-)	-	-	-	-	(+/-)	-	+	-	-	-
Hänninen <i>et al.</i> ³¹⁾	17/-	Y; S; U	15	-	-	-	-	-	+	-	-	-	-	-	-
Sjögren <i>et al.</i> ³²⁾	38/39	Y; B; U	17.1	-	-	-	-	-	-	-	+	-	+	-	+
Sim <i>et al.</i> ²³⁾ b	63/37	A	>10	-	-	-	-	-	-	-	-	-	-	-	+
Akila <i>et al.</i> ³³⁾ c	24/27/28	S; U	NA	-	(+/-)	+	-	-	-	-	-	-	-	-	+
Guo <i>et al.</i> ²⁴⁾	103/64	Y; A; U	16.6	-	-	+	+	-	-	-	-	-	-	-	+
Bast-Pettersen <i>et al.</i> ³⁴⁾	20/20	Y; A; U	8.1	-	-	-	-	-	-	-	+	+	+	+	+
Riihimäki <i>et al.</i> ³⁵⁾ d	30/29/25	S; U	NA	-	-	-	-	-	-	-	-	-	-	-	+
Letzel <i>et al.</i> ²⁵⁾	32/30	Y; P; U	13.7	-	-	-	-	-	-	-	-	-	-	-	-
Iregren <i>et al.</i> ⁴¹⁾ e	119-16-38/39	Y; B; U	15/8/15	-	-	-	-	-	-	-	+	+	-	-	+
Polizzi <i>et al.</i> ²⁶⁾	64/32	Y; S	25.4	-	+	-	+	-	-	-	-	-	-	-	-
He <i>et al.</i> ²⁷⁾	32/34	Y; A; U	14.9	-	-	+	-	-	-	-	-	-	-	-	+
Buchta <i>et al.</i> ³⁶⁾	98/50	Y; A; P; U	6	-	-	-	-	-	-	-	+	-	-	-	-
Buchta <i>et al.</i> ³⁷⁾	44/37	Y; A; P; U	11.4	-	+	-	+	-	-	(+/-)	-	-	-	-	-
Kiesswetter <i>et al.</i> ³⁸⁾ f	20/12	Y; A; P; U	15	-	-	(+/-)	-	-	-	-	-	-	-	-	-
Kiesswetter <i>et al.</i> ³⁹⁾ f	92/50	Y; A; P; U	8.8	-	-	-	-	-	-	-	-	-	-	-	-
Deschamps <i>et al.</i> ⁴²⁾	30/60	Y; A; P; U	6.5	-	-	-	-	-	-	-	-	-	-	-	-
Giorgianni <i>et al.</i> ⁴⁰⁾ g	86/-	Y; A; B	16?	-	-	+	+	+	+	-	-	-	-	-	-
Lu <i>et al.</i> ²⁸⁾	66/70	Y; S	30.2	+	-	-	+	-	-	-	-	-	-	-	+
Zawilla <i>et al.</i> ²⁹⁾	54/51	Y; A; S	21.6	-	+	-	+	+	-	+	-	-	-	-	-
Yang <i>et al.</i> ³⁰⁾	91/184/91	Y; S	21.2	+	-	+	+	-	-	-	-	-	-	-	+
Number of studies with +/-				2+; 13-	5+; 6-	2(+/-); 5-	7+; 1(+/-); 8-	8+; 1-	3+; 3+	1+; 1(+/-); 1-	5+; 1(+/-); 8-	2+; 5-	2+; 5-	2+; 2-	11+; 6-
Numeric sum score				0.13	0.46	0.6	0.5	0.75	1.0	0.5	0.39	0.29	0.29	0.5	0.65

Differences between groups in neuropsychological performance or differences related to exposure parameters: Large/Statistically significant difference $p < 0.05$ +; Differences in the range of $p 0.05-0.10$ (+/-); No difference $p > 0.10$ -.

Type of exposure characterization: Years exposed: Y; Air measurements: A; Blood, including whole blood: B; Serum: S; Plasma: P; Aluminum in Urine: U.

Duration of exposure presented as hours in some studies but otherwise calculated as years of exposure.

Numeric sum score: 1 assigned to +; 0.5 assigned to (+/-); 0 assigned to -.

^a The subjects were recruited by self-selection and were symptomatic workers.

^b Some of the results are also published in Dick *et al.*⁴⁴⁾ The Dick *et al.*⁴⁴⁾ study focuses on tremor, and no tremor was observed. As the Dick *et al.*⁴⁴⁾ study can be regarded as a double publication, it is not included in the table.

^c Akila *et al.*³³⁾ and

^d Riihimäki *et al.*³⁵⁾ published results from the same subjects in a slightly different way. The symptom score is from the Riihimäki *et al.*³⁵⁾ study.

^e Part of the sample, 38 welders and 39 referents, was used in Sjögren *et al.*³²⁾

^f The subjects seem to have been split into two different cohorts based on company (automobile vs trains and trucks). Kiesswetter *et al.*³⁸⁾ is a follow-up of the study by Buchta *et al.*³⁷⁾

Kiesswetter *et al.*³⁹⁾ is a follow-up of Buchta *et al.*³⁶⁾

^g This study exhibits several methodological weaknesses. The presentation of the results in this study is unclear, and it is thus difficult to evaluate the findings.

with three tests (the MMSE, SDMT and Raven's test). The only exposure parameter was the number of years worked⁴³⁾. The exposed workers' performance was poorer than those of the referents. However, according to Cherry⁴⁵⁾, among the exposed subjects, the subjects with the longest duration of exposure had the fewest years of education. Further, the referents had more years of education, and more of them spoke English as their native language, which could have further confounded the results. When the data were reanalyzed, a larger estimated effect was found among miners with a native language other than English⁴⁶⁾. Several of the weaknesses of this study were not well recognized, which led to further studies on possible nervous system effects related to occupational exposure to aluminum.

A study from the former Yugoslavia found slower psychomotor reaction, reduced memory and "disturbance of the mental balance" in workers in an aluminum foundry²⁰⁾. In a study of elderly workers employed in a primary alumi-

num plant, the potroom workers performed less well on a test for tremor²²⁾. Further, there was a tendency to more self-reported symptoms and lower performance in tests for psychomotor tempo and visuospatial organization. In the following years a study by Sim *et al.*²³⁾ as well as a study by Bast-Pettersen *et al.*³⁴⁾ did not find increased tremor among aluminum-exposed workers. However, in the latter, years of exposure to aluminum, but not age, was predictive of poorer performance on the tremor test. There was an association between slower reaction time and aluminum in the air, and the exposed welders reported slightly more symptoms³⁴⁾. Several studies conducted by a German research group did not find increased tremor among workers exposed to aluminum³⁶⁻³⁹⁾.

As shown in Table 1, there was a slight tendency toward findings of impaired information processing speed based on the test results from 13 studies. There were also reports of poor performances on memory tests in four studies,

among which two studies reported weaker performances on verbal and visual memory test for subjects exposed to aluminum, while one study reported effects on verbal memory and another reported effects on only visual memory. A majority of the studies reported symptoms.

Discussions

In this minireview of neuropsychological function associated with occupational exposure to aluminum, there were no clear, consistent findings of occupational aluminum exposure being associated with neuropsychological deficits. Approximately 1,500 workers were included in studies where exposure was assessed in a more “objective” way than via years exposed.

In 2007, Meyer-Baron *et al.*⁴⁷⁾ published a meta-analysis that included nine studies of workers occupationally exposed to aluminum, which together included 449 exposed subjects and 315 referents. Several of the test results indicated worse performances for the exposed group, but the only significant overall effect was for an information processing speed test, the Digit Symbol test. In the present study, the finding of a weak tendency toward impaired information processing speed is consistent with the meta-analysis published by Meyer-Baron *et al.*⁴⁷⁾, but the present study gives only a weak indication that such an association exists.

The finding that few studies reported effects on verbal/academic skills could be explained by the fact that the groups were often matched according to verbal/academic skills. The finding of more symptoms among the exposed groups could be an indication of a possible, slight effect of exposure. However, it might also, like in other studies of neurotoxicants, be related to the fact that the subjects were subjected to thorough examinations, which may have made them more alert to possible symptoms than they might otherwise have been.

Overall, only 24 studies that fulfilled the inclusion criteria were included, which is small considering the number of workers exposed to aluminum and the focus on aluminum in the environment. In addition to this small number of subjects and studies, the types of neuropsychological tests applied varied considerably.

Aspects of Validity

Inclusion criteria

The decision to exclude studies in which *symptom questionnaires* were the only measure of cognitive function was

based on the fact that a symptom questionnaire is not a neuropsychological test. A study of men in manual occupations illustrated that self-reported conceptions of cognitive abilities in occupational and environmental health settings can be trusted to only a limited degree¹⁹⁾.

Inclusion criteria other than those listed in the methods section, such as response rate, were not applied in this minireview. The present study represents more of a “state-of-the-art review” than a “critical review”⁴⁸⁾. Such a state-of-the-art review can be of value for new researchers in this field, and the study could highlight that more research is needed in this field.

Ways of categorizing tests

In this minireview, all tests were categorized as measures of a specific neuropsychological function. However, there are several ways to categorize tests, and while it is obvious what some of the tests measure, it is not for many others.

Some tests can be classified as tests of memory but also as tests of attention/working memory. An example of this is the WAIS subtest Digit Span, which is often categorized as a memory test in older studies; however, it was categorized as an attention/working memory test in this review. The Digit Span Backwards subtest is also classified under executive functioning in some studies.

Use of the term executive function is more complicated. Some tests are regarded as “typical” tests of this function, such as the Wisconsin Card Sorting Test and the Stroop Color/Word Test¹³⁾. However, these tests are often not chosen when designing large studies on exposed subjects, mainly due to the amount of time available. Often, the Trail Making Test B, which is easier to apply, is chosen as a measure of this function, which is in accordance with the classification used in the professional manual Norms for an Expanded Halstead-Reitan Battery¹⁴⁾ and with several other studies in the field of neurotoxicology, such as the meta-analysis of manganese-exposed workers by Meyer-Baron *et al.*⁴⁹⁾

Another problem is the assessment of *tremor*. While evaluations with accelerometers such as the CATSYS Tremor Pen are definite tremor tests, the Kløve-Mathews Static Steadiness Test/Nine Hole Steadiness Test is something of a cross between a tremor test and a test of hand-eye coordination⁵⁰⁾. Other tests, such as those using the EKM⁵¹⁾, which measures precision (hand-eye coordination) and tempo, are categorized in the present study under other motor skills.

As it is important for the groups under study to be similar in terms of cognitive function, the *verbal academic skills*

function is often used as a way of ensuring that the groups are sufficiently similar. However, there is a risk that it will go undiscovered if exposure leads to impairment of this function, for example, if the comparisons between the exposed and unexposed groups are adjusted for the level of verbal academic skills along with age.

In the present study, a simplified scoring system was applied. There was no difference in scoring based on whether the finding was supported by one or by several tests, and only one test for a specific function showing poor performance was taken as evidence that this function was impaired. This may represent a weakness of the study, as several tests for a specific function might have been an indication of a stronger association between exposure and effects. However, there are many reasons for including a limited number of neuropsychological tests in a study, with the most obvious being that neuropsychological testing is time consuming, and often the workers do not have the opportunity to be away from the workplace for a long time.

Does occupational exposure to aluminum increase the risk of developing impaired cognitive function?

The question of whether occupational exposure to aluminum can increase the risk of developing severe neurological disease is still unresolved. A recent study found that miners who were exposed to respirable aluminum had elevated rates of Parkinson's disease. The miners exposed to respirable aluminum did not have an elevated incidence rate of Alzheimer's disease. However, when a broader category of Alzheimer's disease and other dementias was applied, the exposed miners did have an increased risk of the disease category of Alzheimer's disease with other dementias⁵².

The present study focused on anticipated subtle functional impairments of the nervous system, and the study found modest findings on the relation of neuropsychological impairment to aluminum exposure. However, even small effects that can be attributed to exposure to aluminum are of interest because aluminum, as the third most abundant element on earth, is such an important environmental facet. We do not know whether aluminum can lead to greater health risks related to nervous system function in some groups (older persons, those with certain illnesses, premature infants receiving parenteral nutrition), with the exception of patients with renal failure. The existing studies are too few to provide a conclusive answer regarding whether occupational exposure to aluminum represents an increased risk of damage to the nervous system in the form of impaired cognitive function.

Conclusions

No clear, consistent findings of occupational aluminum exposure being associated with neuropsychological deficits emerged after summarizing the results of the 24 studies included in the analysis. There was a slight tendency toward weaker performances on tests of information processing speed and memory.

At present, the limited number of studies in this field makes it difficult to draw a clear conclusion as to whether occupational exposure to aluminum implies an increased risk of altered neuropsychological function, and more research in this field is needed.

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