[Translated by Julian Brooke and published with the concurrence of Industrial Health and Occupational Diseases 2001;27(6):346-8.]

RESEARCH ON THE NEUROBEHAVIORAL FUNCTION OF WORKERS OCCUPATIONALLY EXPOSED TO FLUORIDE

Zhiyong Guo,[a] Yuhua He,[a] Qixing Zhu[a]

Hefei, China

[SUMMARY: Sixty-five operations workers (all males) in an electrolytic aluminum production facility were divided into two groups. The first group of 37 was employed for more than 5 years, and the second group of 28 for 5 years or less. These men had no history of liver, kidney, or immune-related disease. X-ray tests indicated that they were not suffering from occupational fluorosis (according to the standards of GB3234-82). For controls, 52 males from the service departments with no history of exposure to fluoride were used as controls. Neurobehavioral function of the long-exposure group measured by the neurobehavioral core test battery (NCTB) revealed, with the exception of the Benton visual retention measurement, diminished performance for every testing index as compared to the controls. Even the scores for emotional state of the short exposure group were markedly lower than for the control. By relating these test results to fluoride exposure, our study demonstrated various effects of occupational fluoride exposure on the central nervous system, thereby providing early warning indicators that can be used to protect the health of workers who have occupational contact with fluoride.]

[Keywords: Aluminum production; Central nervous system; Fluoride-exposed workers; Magnesium fluoride; Neurobehavioral core test battery; Occupational fluoride exposure.]

INTRODUCTION

Although fluoride is considered by many to be an essential trace element, its excessive intake causes obvious damage not only to the skeletal system but also to the non-skeletal organ system. In recent years, the damage fluoride inflicts on non-skeletal organs, and in particular the nervous system, has received a great deal of attention.[1] However, research on the effects of fluoride on neurobehavioral function (as measured by the neurobehavioral core test battery, or NCTB) is new to the literature. By relating NCTB to fluoride exposure, the purpose of this study was to investigate the effects of occupational fluoride exposure on the central nervous system and to determine to what extent the level of exposure correlates with those effects and hopefully thereby provide early warning indicators that can be used to protect the health of workers who have occupational contact with fluoride.

MATERIALS AND METHODS

Fluoride exposure: The production of aluminum from alumina in the factory under study uses fused-salt electrolysis of aluminum oxide; the fluxing agent is cryolite (Na_3AlF_6) together with small amounts of magnesium fluoride (MgF_2). Fluoride is emitted from the electrolytic units into the air in the form of a gas, mist, or dust. Protective measures are mostly limited to natural and artificial ventilation. Over the past ten years, the geometric mean of fluoride concentration in the factory air was found to be 0.82 mg/m^3 (with a range of 0.14 to 5.9 mg/m^3). The

[a]School of Public Health, Anwei Medical University, Anwei, Hefei 230032, China.

national health standard of 1 mg F/m^3 in *Health Standards Designated for Industrial Enterprises* TJ39-79 is exceeded by these levels 24.7% of the time.

Selection and grouping of subjects: The fluoride-exposed subjects were the 65 factory floor workers who carry out the aluminum electrolysis. All the workers were healthy males with no history of liver, kidney, or immune-related disease. X-ray tests indicated they were not suffering from occupational fluorosis (according to the standards of GB3234-82). These workers were divided into groups based on the length of time they had been employed at the factory: 37 were in the > 5 years group (long exposure group) and 28 in the ≤ 5 years group (short exposure group). The control group was selected from 52 male employees working in the service department with no history of relevant exposure. The average age of the fluoride-exposed groups was 29.6 ± 4.4, and the average age of the non-exposed group was 27.9 ± 5.9. The results of surveys demonstrated the two groups were comparable with regard to age, time on the job, and education, as well as tobacco and alcohol consumption, with no family history of mental illness, and no prolonged use of sedatives.

Indices and data collection methods:

Measurement of urine fluoride and serum fluoride: For each worker, urine samples were taken from the first urination of the day, and the fluoride concentration tested. Blood was taken from a vein in the arm below the elbow, and the serum was separated out and tested. A fluoride ion selective electrode method was used for testing in both cases.

Neurobehavioral function testing: The WHO-recommend NCTB (which includes a mood questionnaire as well as motor skills testing) was used to test the neurobehavioral function of both exposed and non-exposed workers.[3]

*Data processing:*The collected data were entered into a FoxPro database, and the NCTB results and other indices were normalized. Then SPSS was used to carry out a statistical analysis.

RESULTS

Urine and serum fluoride levels of workers: The concentrations of fluoride in the blood serum and urine of both the exposed worker groups were clearly higher than the control, and the differences were very significant ($p<0.001$, Table 1).

Table 1. Urine and serum fluoride of workers (mean±SD)

Group	n	Serum fluoride (mg/L)	Urine fluoride (mg/L)
Long Exposure	37	0.074±0.011*†	0.994±0.339*
Short Exposure	28	0.066±0.008*	1.012±0.390
Control	52	0.035±0.007	0.687±0.258

*$p<0.001$ compared to control, †$p<0.01$ compared to short exposure group.

Among the exposed workers, the serum fluoride of the long exposure group was markedly higher than in the short exposure group ($p<0.01$). However, there was no significant difference between the urine fluoride of the two groups ($p>0.05$).

NCTB testing: With the exception of visual retention, the long exposure group showed clearly diminished performance for every testing index as compared to the control. In regard to the scores for emotional state, simple reaction time, digital span, Santa Ana dexterity, and pursuit aiming, the short exposure group was markedly lower than the control. Compared with the short exposure group, the emotional confusion and pursuit aiming error indices of the high exposure group are clearly lower ($p<0.05$), and most of the remaining indices show an overall negative tendency, however this general result is not statistically significant ($p>0.05$, Table 2)

Table 2. Comparison of NCTB results between exposed and non-exposed subjects (mean ±SD)

Index	Fluoride exposed groups		Non-exposed control group (n=52)
	Long exposure (n=37)	Short exposure (n=28)	
Emotional State			
Tension	45.30±9.62**	47.05±11.87**	54.70±8.08
Depression	46.33±9.55**	47.19±12.65**	54.32±8.60
Hostility	45.08±12.24**	46.63±8.59**	55.50±7.71
Vigor	45.03±10.62**	46.97±7.14**	55.34±7.48
Fatigue	43.33±9.18**	45.22±8.56**	57.16±6.57
Confusion	43.22±8.50†**	48.35±9.48**	55.06±8.99
Simple Reaction Time			
Average	47.03±12.94*	49.70±6.18	52.40±8.69
Fastest	47.81±12.59*	48.70±7.06*	52.38±8.93
Slowest	48.86±6.81	50.37±4.34	50.74±13.56
Digit Span	46.37±8.99**	48.41±8.44*	53.14±10.91
Santa Ana Dexterity			
Preferred Hand	47.27±8.55**	47.26±11.91**	53.44±9.14
Non-Preferred Hand	47.61±9.71**	47.26±9.07**	52.92±10.18
Digit Symbol	47.27±8.33*	51.85±10.26	50.98±10.94
Benton Visual Retention	49.54±9.43	49.26±10.02	51.62±8.54
Pursuit Aiming			
Correct	49.68±4.16	50.78±5.12	49.78±14.46
Errors	46.41±4.79†**	50.35±4.12	51.74±6.84
Total	48.57±6.87*	48.35±8.32*	51.89±8.72

*p<0.05, **p<0.01 (exposed groups compared to control); †p<0.05 (long exposure group compared to short exposure group).

Table 3. Correlation of relevant NCTB indices with worker serum fluoride

X	Y	Regression equation	*R*	*t*	p
Serum fluoride	Fastest Reaction Time	Y=53.39 – 64.49X	– 0.1593	1.709	<0.05
Serum fluoride	Digit Span	Y=55.78 – 117.70X	– 0.2741	3.017	<0.01
Serum fluoride	Pursuit Aiming Total	Y =53.35 – 69.41X	– 0.2277	2.475	<0.05
Serum fluoride	Santa Ana (PH)	Y=55.45 – 111.46X	– 0.2591	2.839	<0.01
Serum fluoride	Santa Ana (NPH)	Y=55.01 – 103.70X	– 0.2418	2.637	<0.01
Serum fluoride	Tension	Y=58.76 – 178.63S	– 0.4190	4.883	<0.001
Serum fluoride	Depression	Y=58.48 –170.44S	– 0.3919	4.508	<0.001
Serum fluoride	Hostility	Y=59.16 – 186.21X	– 0.4339	5.096	<0.001
Serum fluoride	Vigor	Y=58.81 – 197.20X	– 0.4214	4.918	<0.001
Serum fluoride	Fatigue	Y=63.14 – 367.38X	– 0.6199	8.360	<0.001
Serum fluoride	Confusion	Y=59.28 – 187.30X	– 0.4316	5.064	<0.001

Correlation of NCTB indices and fluoride exposure levels: Except for visual retention and digital decoding, serum blood levels of fluoride were inversely correlated with the normalized NCTB indices (Table 3).

DISCUSSION

This study showed a significant increase in the urine and serum fluoride levels of the exposed workers as compared to the controls, suggesting that the concentration of fluoride in both the blood serum and in the urine can reflect exposure to fluoride. However, serum fluoride is the more accurate indicator of the body burden of fluoride and fluoride metabolism. The reason for this probably lies in factors that influence the concentration of fluoride in urine are more varied than those for blood fluoride, i.e., the intake of food, water, and other liquids (particularly tea) as well as sweating.[4]

In recent years, the toxic effects of fluoride on the nervous system have begun to receive the attention of researchers.[5] Patients suffering from endemic fluoride poisoning show central nervous system deficits such as poor memory, unstable emotions, headaches, imbalances, etc. These symptoms suggest that fluoride may have a direct, toxic effect on the central nervous system.[1] The results of the NCTB testing in this investigation revealed significant differences among the fluoride-exposed groups for various indices as compared to reference standards and the controls, with particular deficits in attention, auditory retention, and physical dexterity and acuity as well as abnormal emotional states. These findings are consistent with the symptoms of endemic fluoride poisoning, suggesting occupational exposure to fluoride has harmful effects on the higher functions of the central nervous system, negatively influencing both cognitive and autonomic functioning. There is a definite relationship between the damage caused by fluoride and the level of exposure.

The correlation analysis shows that, with the exception of visual retention and digit symbol testing, serum fluoride is negatively correlated with all relevant indices, further demonstrating the cause-and-effect relationship between occupational fluoride exposure and neurobehavioral function; these tests can therefore be used as early indicators to help protect the health of workers exposed to fluoride as part of their jobs.

REFERENCES

1 Ta Yulin. The effects of fluoride on body metabolism and various organ systems. Chinese Journal of Control of Endemic Disease 1994;9(3):163-8.
2 Zhang Haimou, Tan Liang, Liu Jiandong, et al. Research into methods for testing fluoride concentration in tiny samples of urine and blood serum. Chinese Journal of Health Laboratory Technology 1997;7(5):259-62.
3 Liang Youxin. An introduction to the battery of neurobehavioral tests recommended by the WHO. Industrial Health and Occupational Diseases 1987;13:331-9
4 He Fengsheng, editor. Chinese Occupational Medicine. Beijing: People's Medical Publishing House; 1999. p. 383-4.
5 Xiao Jianxiao, Yu Sheng. The effects of fluoride on the nervous system. Journal of Environment and Health 1997;14:141-3.