

BEHAVIORAL CHANGES AND GENERAL TOXICITY IN RATS AFTER SUBCHRONIC INORGANIC ARSENIC AND FLUORIDE TREATMENT



Kitti Sárközi, Zsuzsanna Máté, Tünde Vezér, András Papp



Department of Public Health, University of Szeged Faculty of Medicine, Szeged, Hungary

Introduction

ARSENIC (As)

General population exposure

- groundwater impurities
- contaminated drinking water and food

Occupational exposure

- mining
- smelting
- glass industry
- microelectronics

Toxicity

- central and peripheral nervous system abnormalities: neuropathy, headaches, weakness, mental confusion
- cancer (liver, lung, skin, kidney), hyperkeratosis, hair loss, cyanosis, blackfoot disease, anaemia

FLUORINE (F)

General population exposure

- groundwater impurities
- contaminated drinking water and food

Occupational exposure

- aluminium metallurgy
- automotive industry
- microelectronics

Toxicity

- dental and skeletal fluorosis
- neurological deficits: headache, tremors, tetanic contractions, muscle weakness

Materials and Methods

7 weeks old adult male Crl: WI BR Wistar rats (160 ± 20 g, 4 groups of 12 rats each) were treated with sodium (meta)arsenite, sodium fluoride and their combinations per os by gavage, 5 days a week, once a day for 6 weeks.

Treatment groups and doses

GROUP CODES	DOSE AND TREATMENT
Control	distilled water, per os
As	NaAsO ₂ , 10 mg/kg b.w. per os
As+F	NaF, 5 mg/kg b.w. per os
F	NaAsO ₂ 10 mg/kg b.w.+ NaF 5 mg/kg b.w. per os



General toxicological investigation

During the treatment period, body weight and food and water consumption was measured every day. At the end of the 6 weeks treatment, 6 animals in each group were dissected and organ weights were measured. The other 6 rats in each group were kept for 6 more weeks without any treatment and at the end of the 12th week they were also dissected and the organ weights were measured.

Behavioral toxicological investigation - spontaneous locomotor activity

Open field (OF) test was done in the 2nd, 4th, 6th, 8th, 10th and 12th weeks

Open field box, CONDUCTA, Experimetria, Hungary

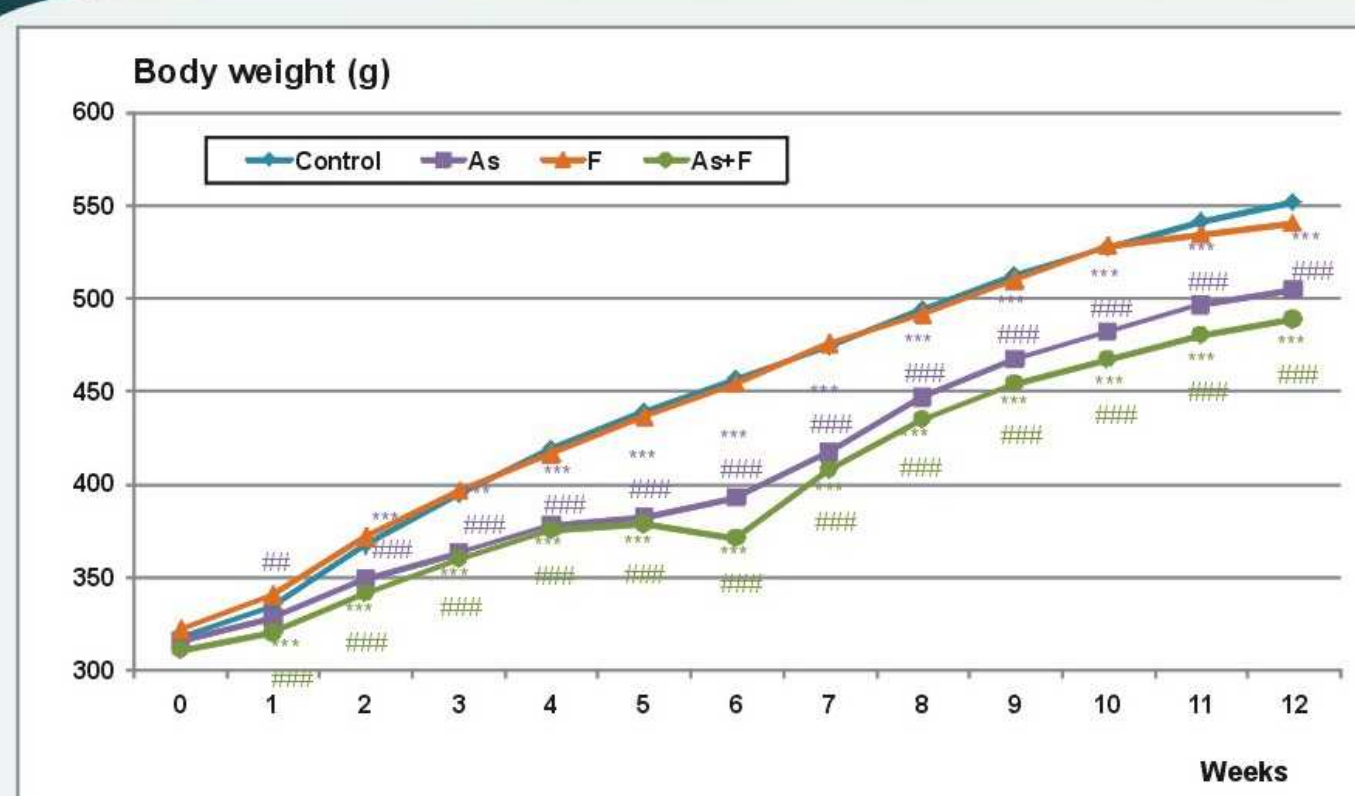
10 min/rat/test; motility parameters - ambulation distance, time and count; rearing time and count; local time and count; immobility time and count

Arsenic level of the samples was measured by inductively coupled plasma mass spectrometry.

The data were analysed by one-way ANOVA. Post hoc analysis of group differences was performed by Scheffe test, with probability level at $p < 0.05$.

Results

General toxicological parameters



Weekly body weight gain was significantly reduced in the As (vs. F) and As+F (vs. Control and F) groups already in the first week. This difference was seen during the whole treatment period, and was more prominent from the second week (As and As+F vs. Control and F). In the post-treatment period food consumption of the rats that had As treatment was increased, but the body weight difference between As and As+F vs. Control and F remained up to the end of the experiment.

Marking of significance

*, **, *** $p < 0.05$; 0.01; 0.001 As, As+F, F vs. Control
#, ##, ### $p < 0.05$; 0.01; 0.001 As, As+F vs. F

Food and water consumption in the As and As+F groups was significantly reduced (vs. Control and F) during the treatment period. When the treatment was over, food and water consumption increased in the As and As+F groups but it was no more different from that in Control and F groups.

Arsenic levels ($\mu\text{g/kg}$)

GROUPS	Control (12 th week)	As+ (group As, 6 th week)	As- (group As, 12 th week)
Blood	22658.16 ± 2280.61	1580522.26 ± 29587.83 *** ###	753059.95 ± 51397.44 ***
Liver	1811.46 ± 574.05	225456.89 ± 30588.90 *** ###	40897.24 ± 6428.51
Cortex	936.53 ± 284.08	136840.49 ± 41343.36 ** #	45387.70 ± 18128.90

As+: As-treated group (1-6 weeks)

As-: post-treatment As group (7-12 weeks)

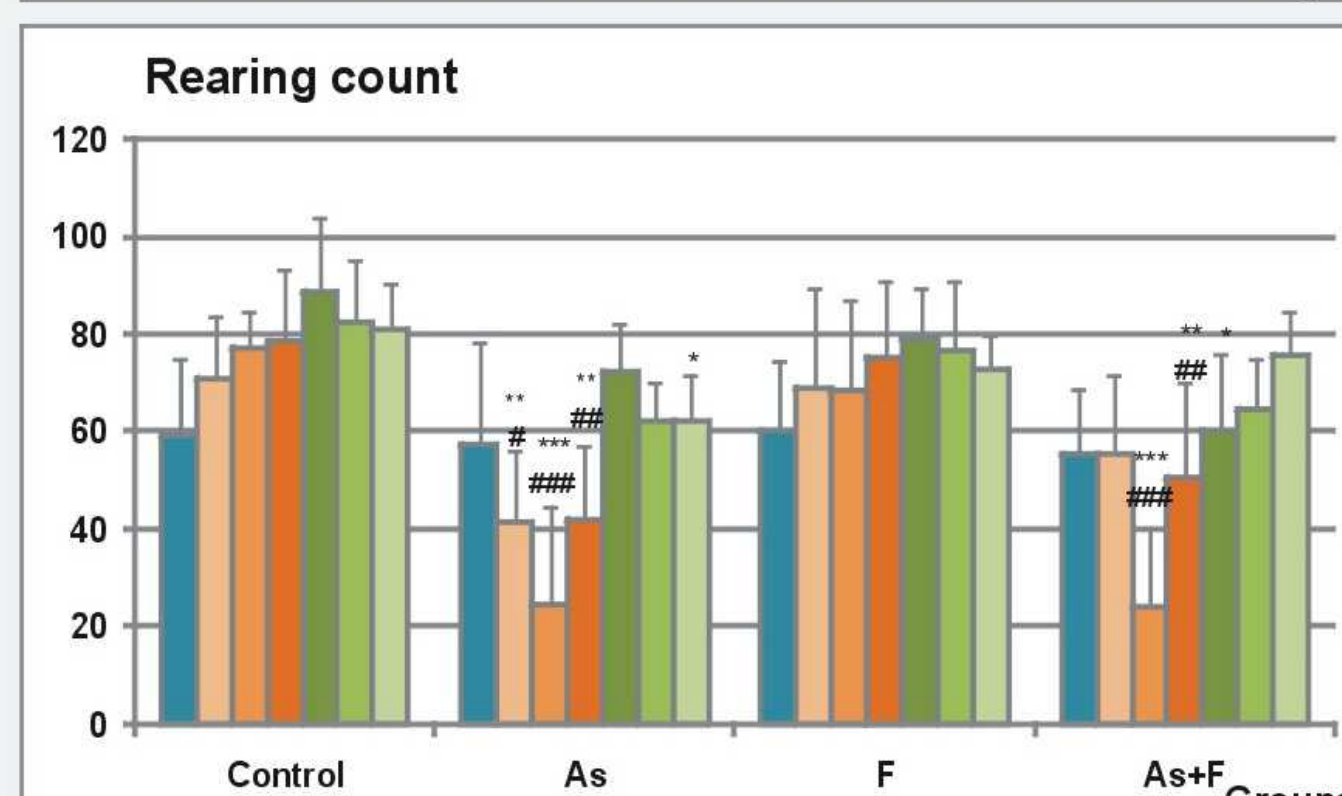
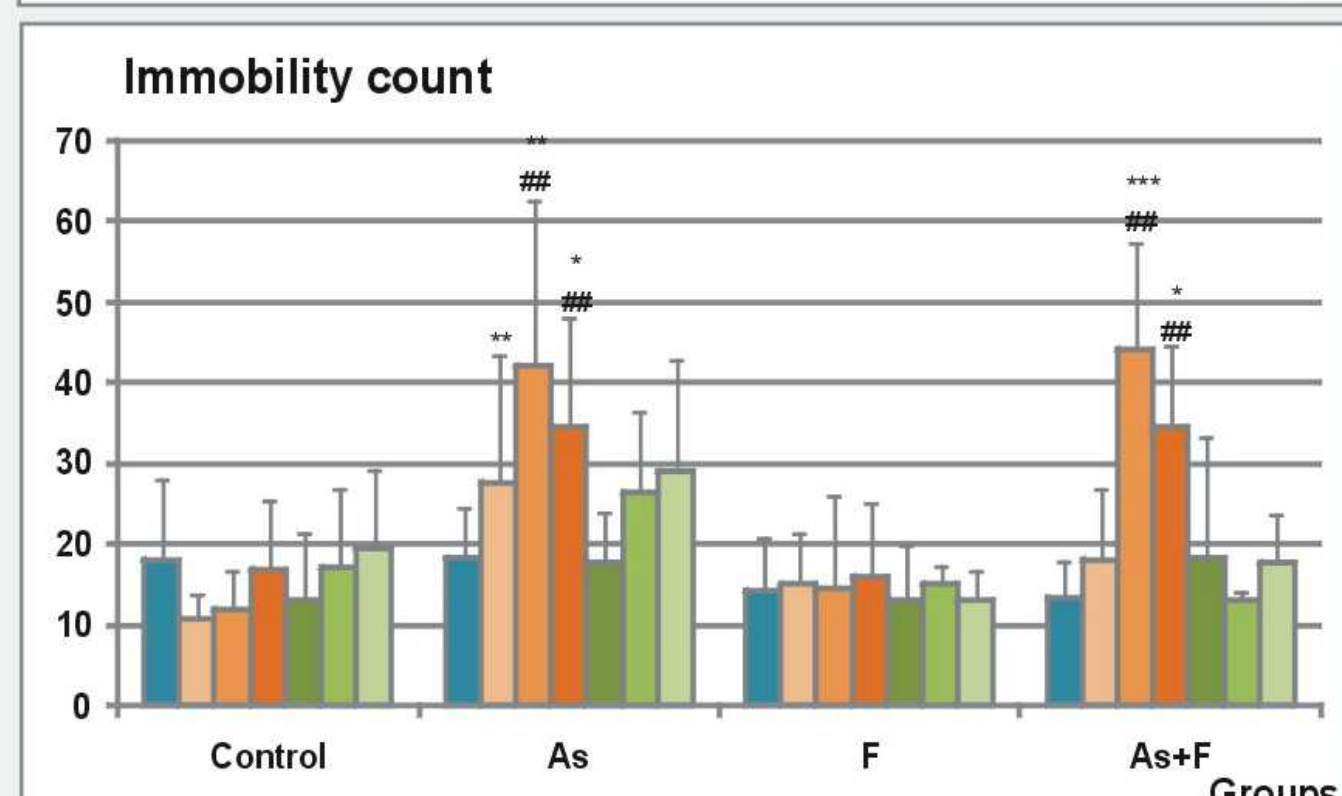
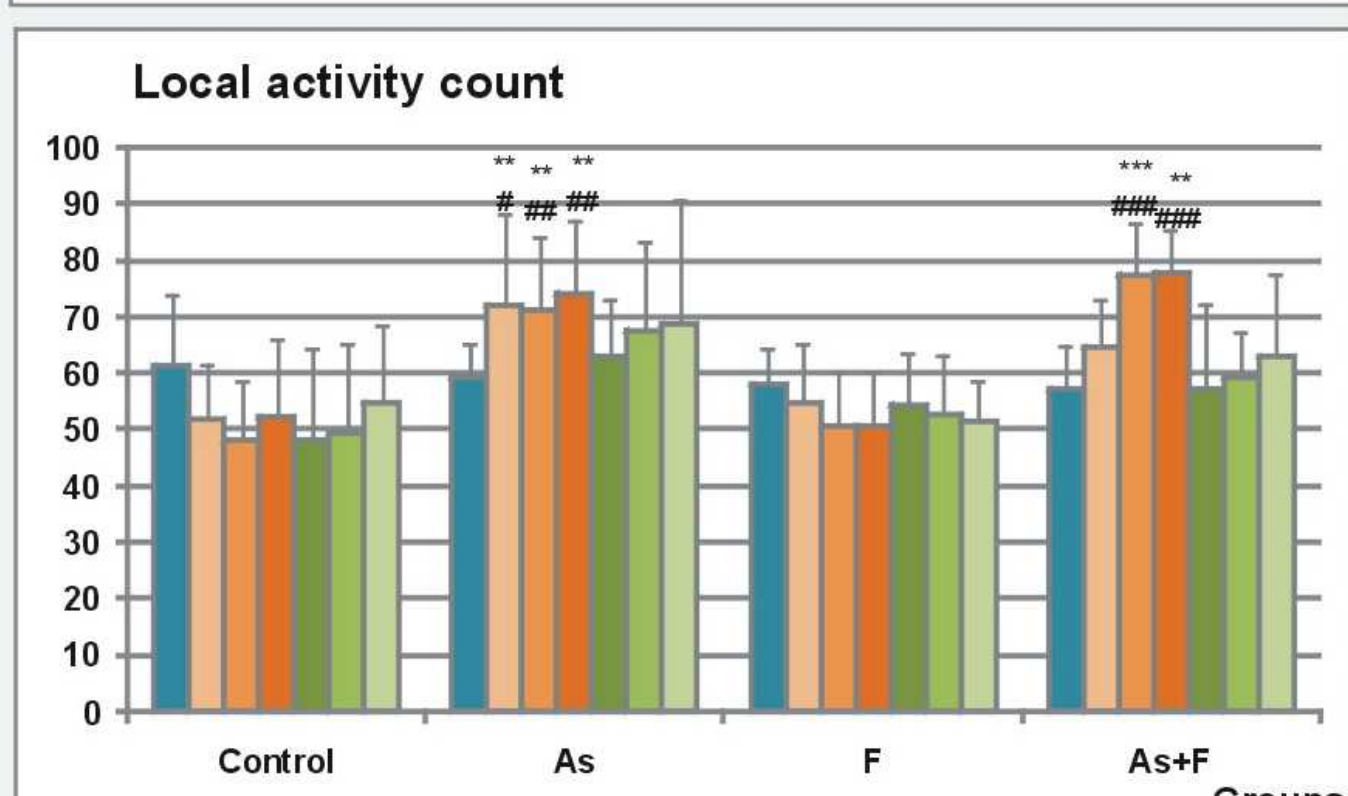
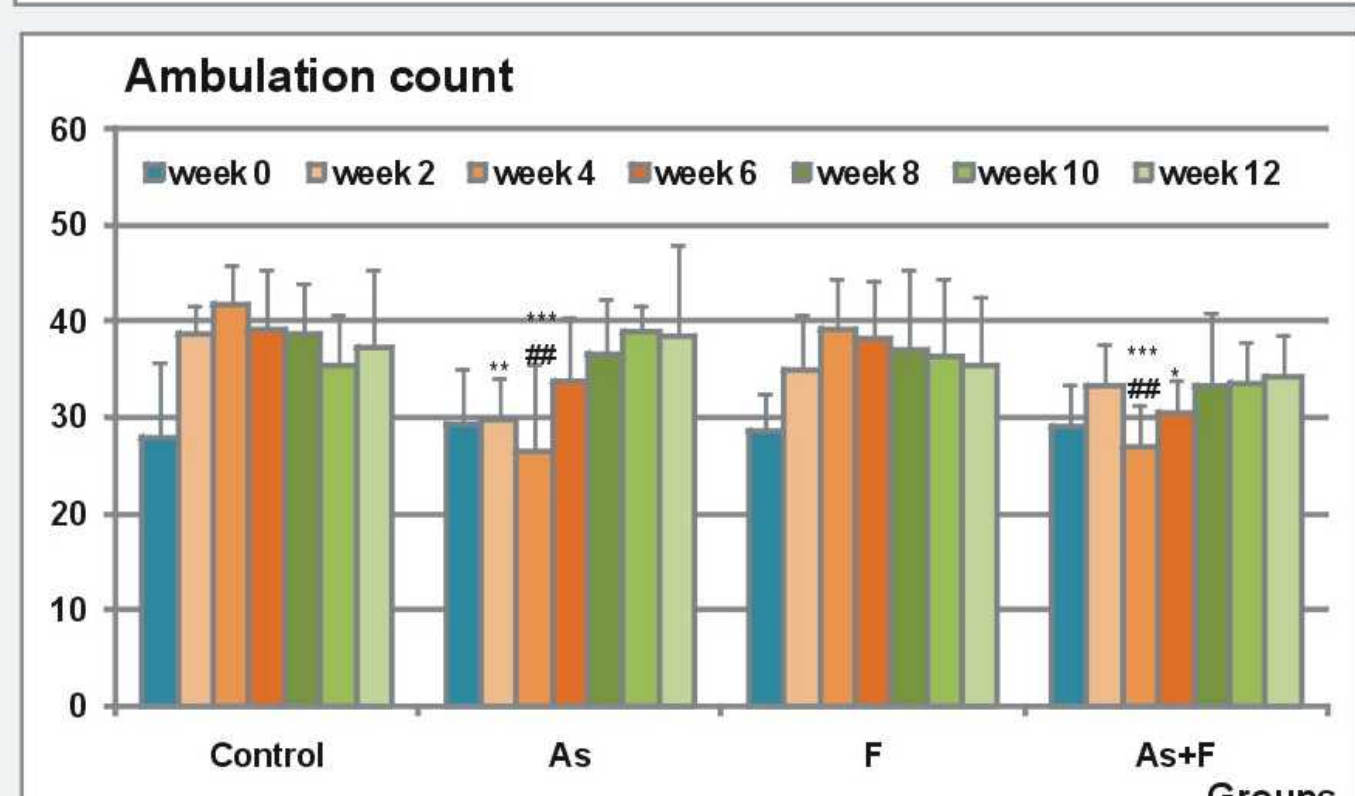
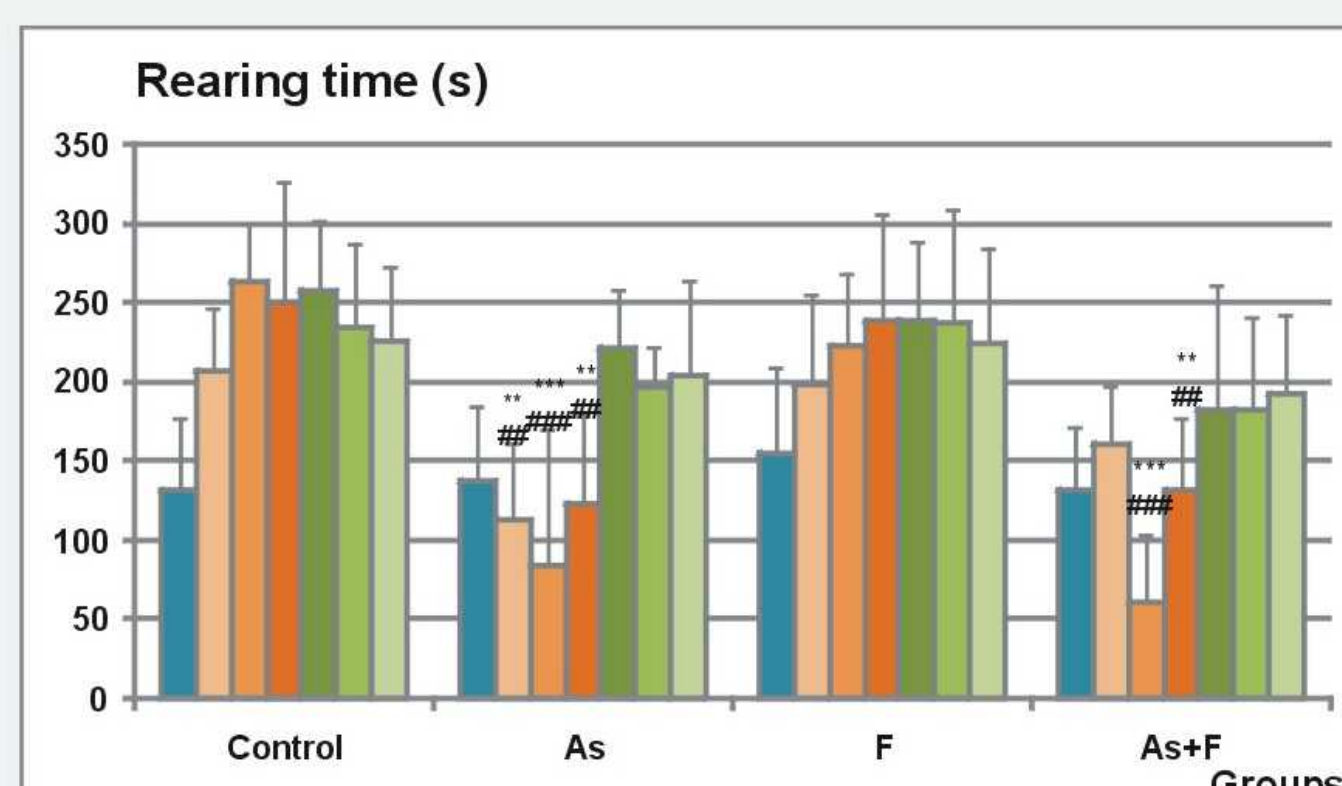
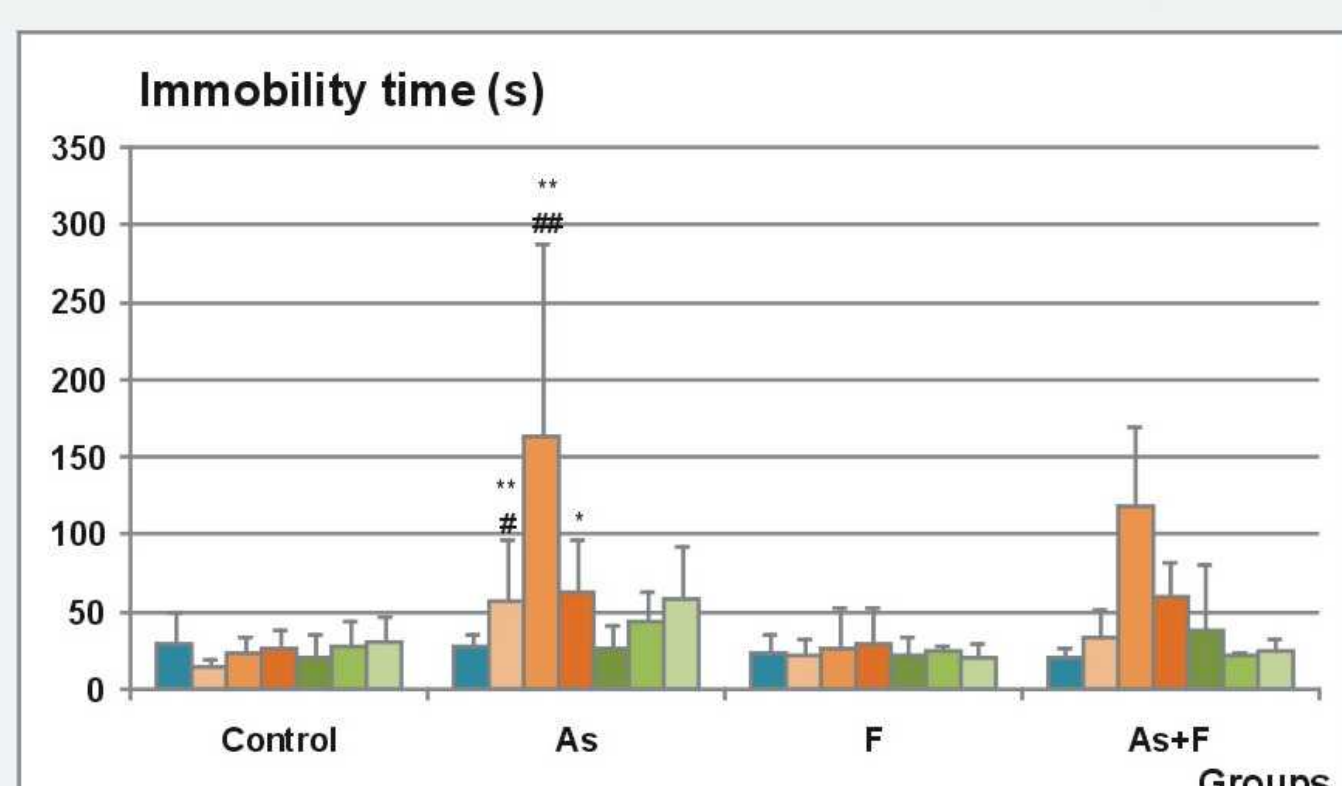
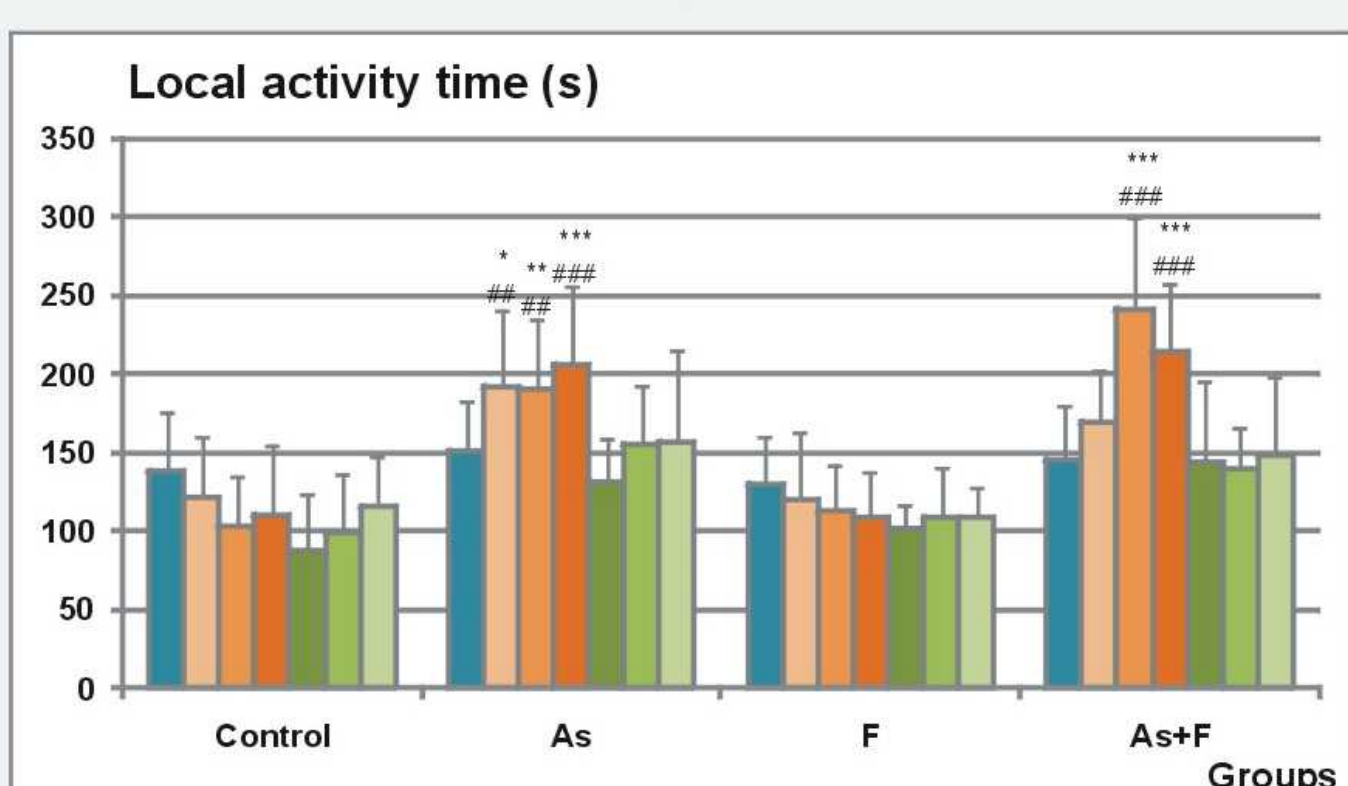
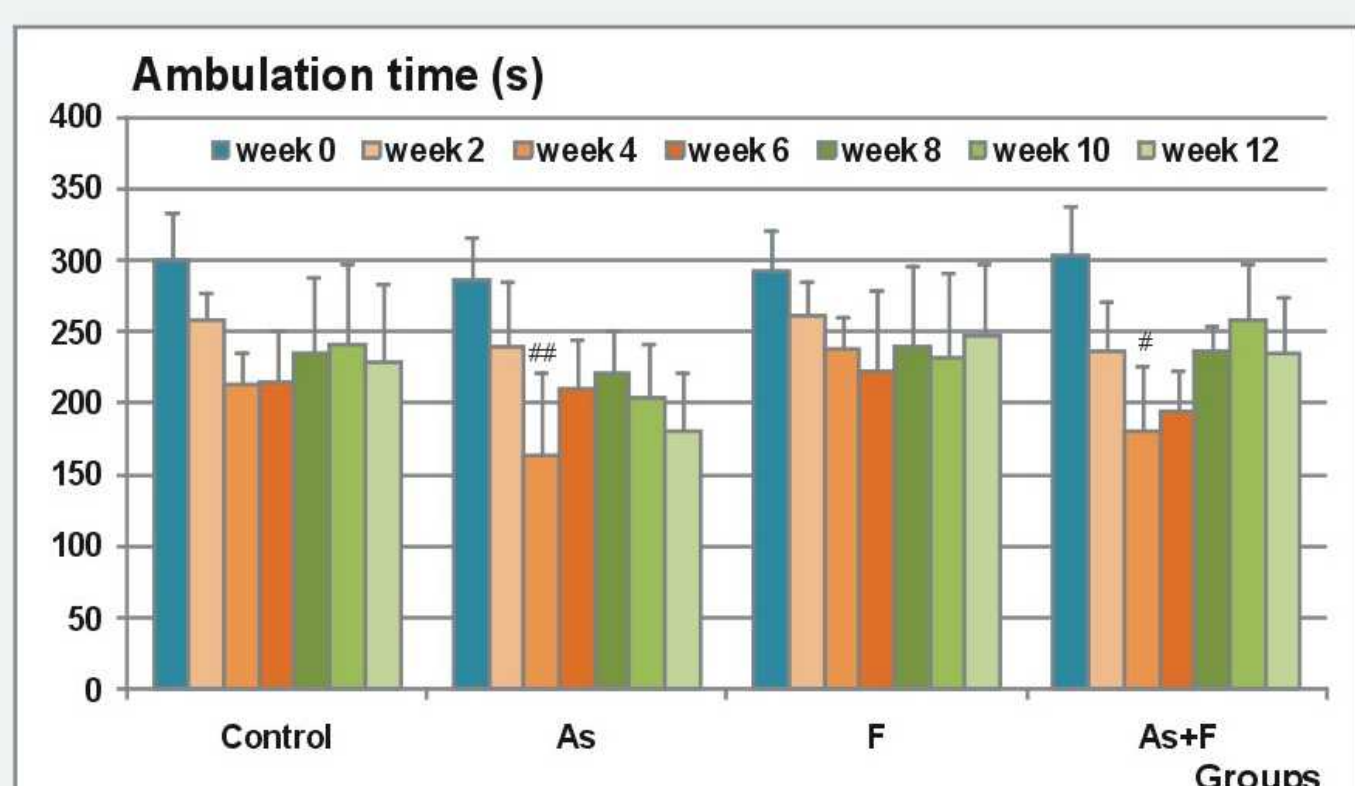
*, **, *** $p < 0.05$; 0.01; 0.001 As+, As- vs. Control

#, ##, ### $p < 0.05$; 0.01; 0.001 As+ vs. As-

During the treatment period As concentration in the blood, liver and cortex was significantly elevated in As group compared to Control. In the 6 weeks without treatment arsenic was partly eliminated.

Behavioral toxicological investigations

Open field test in the 2nd, 4th, 6th, 8th, 10th and 12th weeks. Time and count of the activity forms.



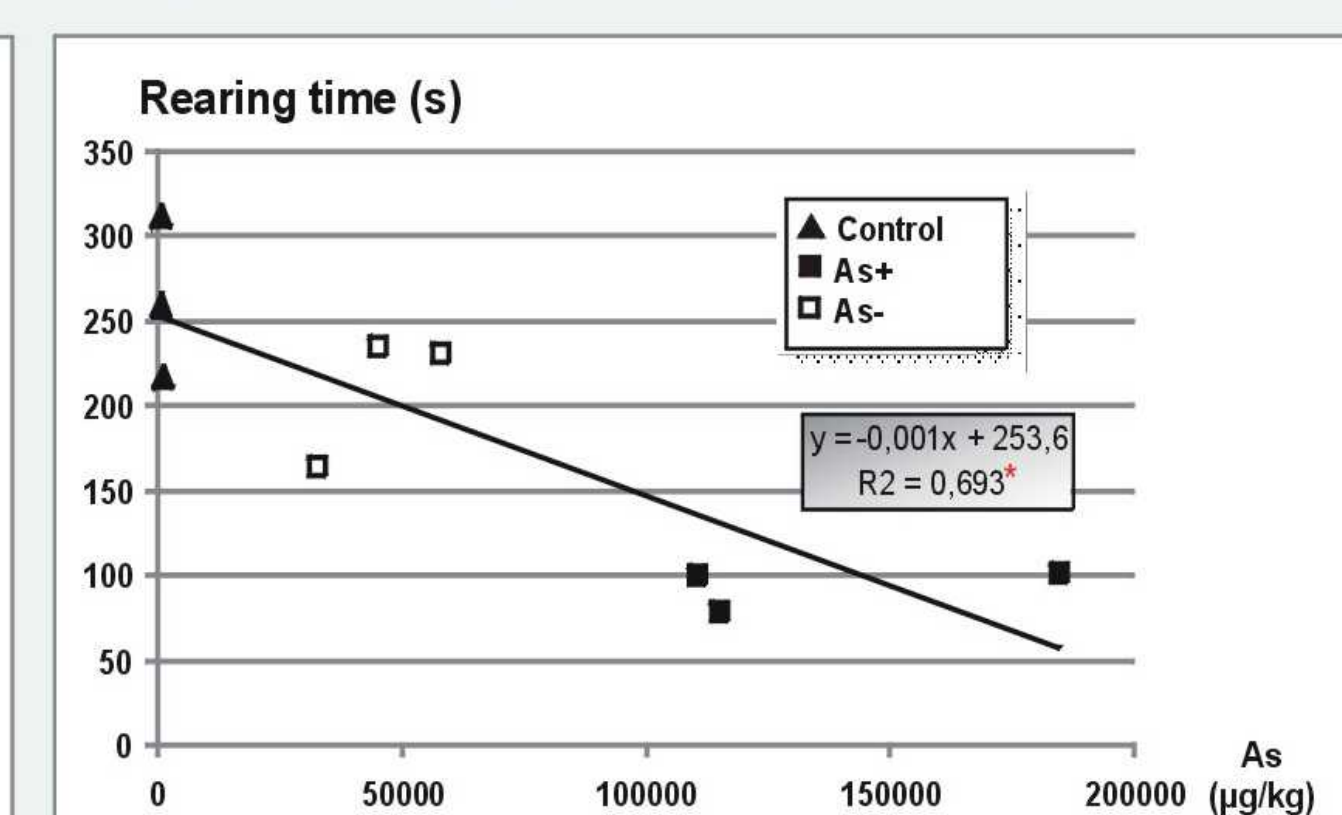
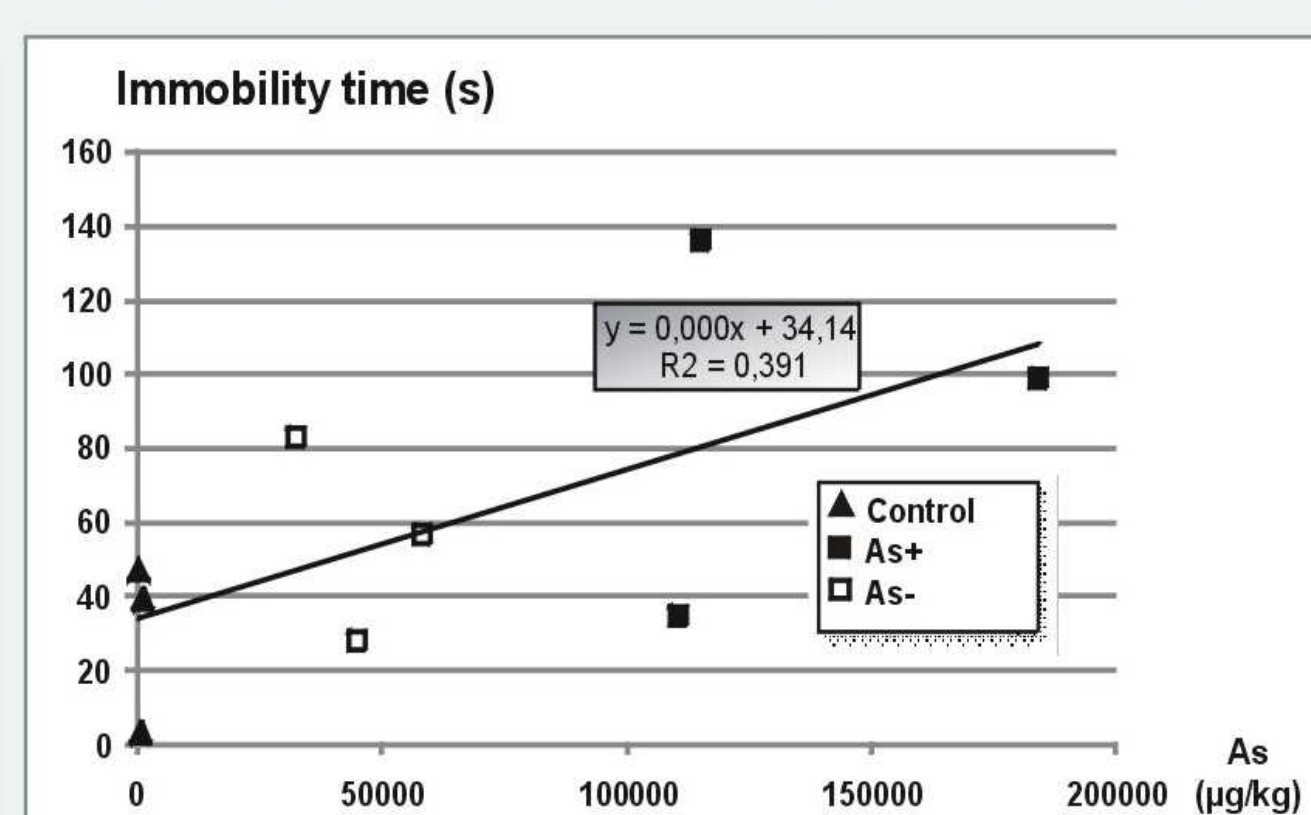
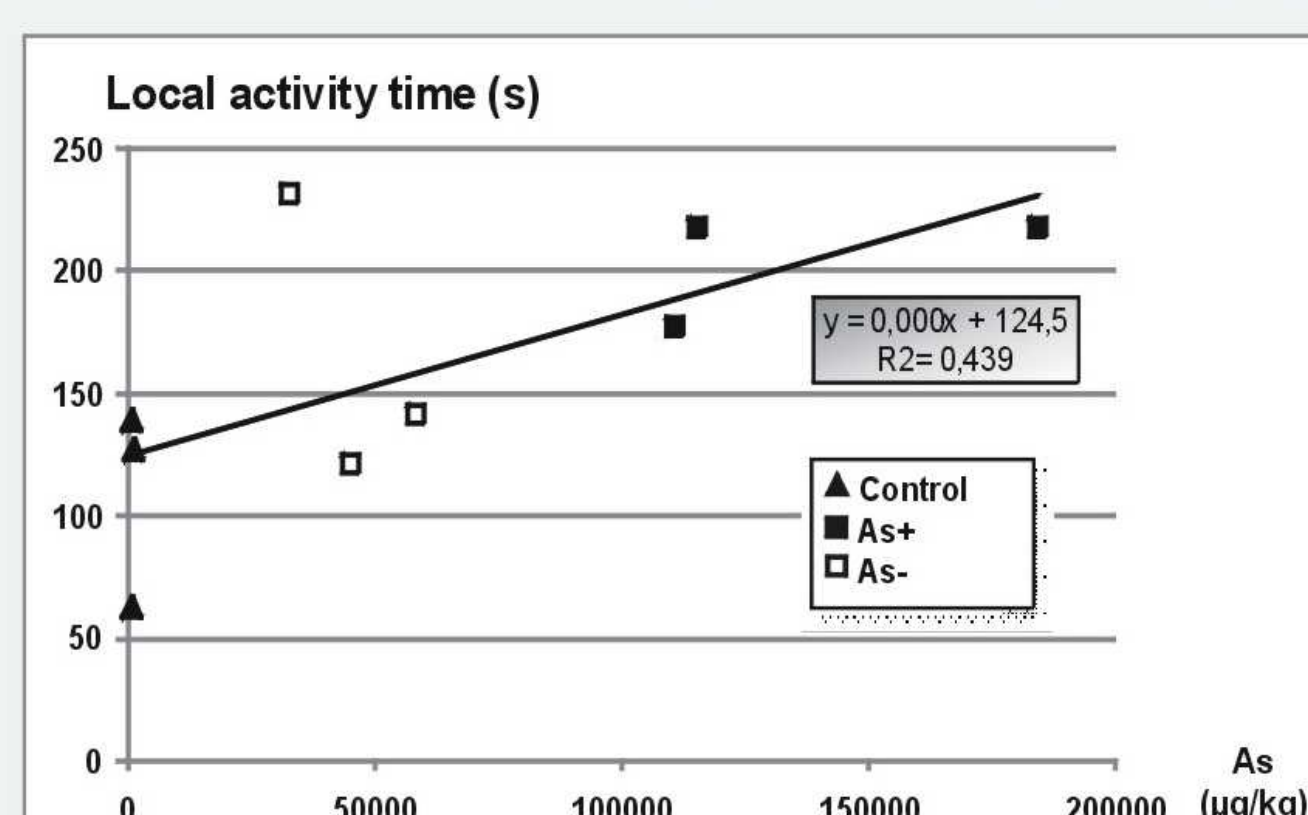
The effect of As and F on OF motility were quite different. In the As-treatment period, both in the 4th and the 6th week, As and As+F caused significant decrease in motility: time and event count of rearing and ambulation decreased while the same indicators of immobility and local activity increased, vs. both Control and F. In the post-treatment period, there was no significant difference between the groups except in the rearing count. Some of the open field parameters were well correlated with the individual rats' cortical arsenic level. For rearing time the correlation was significant.



Conclusion

In the treatment scheme applied, significant effects on both general and behavioral endpoints by As, but not by F, were detected. In the groups receiving As, significant increase of the time spent with local activity and immobility, and significant decrease of vertical activity, indicated that the central nervous system was affected by As. Furthermore, F might have an influence on As toxicity. In the post-treatment period, previous As-treatment caused no significant effect on the open field parameters most probably because of the partial elimination of As from the rats' organism. Our results underline the risk from environmental exposure, and, together with the lack of effect of F (contradicting literature data) point to the need of further investigation.

Correlation of the cortex As level to local activity, immobility and rearing time.



* $p < 0.05$ for the linear fit