

Neurotoxicity of styrene in occupational and experimental exposure

by ANNA MARIA SEPPÄLÄINEN M.D.¹

SEPPÄLÄINEN, A. M. Neurotoxicity of styrene in occupational and experimental exposure. *Scand. j. work environ. & health* 4 (1978): suppl. 2, 181—183. Occupational styrene exposure caused an increased frequency of abnormal electroencephalograms which correlated to degree of exposure. No dose-response relationship could be shown concerning a slowing of nerve conduction velocities in workers exposed to styrene. Experimental exposure of rats to 300 ppm of styrene caused a transient increase in the nerve conduction velocity in 6 weeks, but in a comparison to control rats no difference was found in measurements performed on rats exposed for 8 and 11 weeks.

Key words: electroencephalography, electroneurography, experimental exposure, occupational exposure, styrene.

Irritative symptoms of mucous membranes are the first ones to appear in acute styrene exposure, although higher concentrations can induce prenarctic symptoms like nausea and dizziness. Long-term occupational exposure to styrene in the reinforced plastics industry caused a clear increase of various symptoms in comparison to nonexposed workers in a Finnish symptom survey made by Härkönen (1). These symptoms included fatigue and concentration difficulties, which may reflect neurotoxic effects. Although individual symptoms or symptom complexes did not show an exposure-response relationship, the connection between symptoms and styrene exposure seemed clear.

The electroencephalograms (EEGs) of 96 male workers occupationally exposed to styrene in the reinforced plastics industry from 0.5 to 14 years, mean 5

years, were interpreted without knowledge of the exposure level (3). Twenty-three of the studied workers had abnormal EEGs; this frequency is higher than would be expected in a normal population. Around 10 % of the general adult population shows abnormal slow or paroxysmal activity according to the EEG literature, and based on this assumption the difference between styrene exposed workers and a normal population is significant ($p < 0.01$, binomial distribution). The time-weighted average styrene exposure during the workday can be reliably monitored by the measurement of urinary mandelic acid concentration. If the mandelic acid concentration exceeded 700 mg/l, one-third of the workers had abnormal EEGs, while only 10 % of the workers with a lower exposure level showed abnormal findings. Workers with a long exposure did not have abnormal EEGs more often than those with short exposure.

Biochemical studies by Savolainen and Pfäffli (2) have shown marked styrene

¹ Department of Occupational Medicine, Institute of Occupational Health, Helsinki, Finland.

accumulation in the brain and perinephric fat of rats exposed to 300 ppm of styrene. This accumulation was accompanied by statistically significant, although mild, biochemical alterations in the brain. Furthermore, these experimental studies suggested that metabolic adaptation takes place. If the same phenomenon occurs in humans, it could explain why EEG abnormalities appear during the first year of exposure and do not increase, or may even decrease, thereafter in those who continue their work.

Nerve conduction velocities, i.e., the maximal motor conduction velocity of the median, ulnar, deep peroneal and posterior tibial nerves, the conduction velocity of the slower motor fibers of the ulnar and deep peroneal nerves and the sensory conduction velocity of the median and ulnar nerves (all measured with skin electrodes), of 40 styrene-exposed workers did not differ as a group from those of normal nonexposed persons with a similar age distribution. However, nine of the exposed workers had abnormally low conduction velocities in one (5 cases) or more (4 cases) nerves. In two cases with mononeuropathy another etiology could be ascertained, and in two other cases another etiology was strongly suspected. One case had alcoholic polyneuropathy. Thus in three cases of polyneuropathy and one of mononeuropathy no other etiology was found. The exposure of these subjects was relatively low at the time of the examination, and therefore it was difficult to ascertain a causal relationship between styrene exposure and neuropathy at an exposure level which had seldom exceeded 100 ppm.

For the further study of the peripheral nervous effects of styrene, an experimental study was conducted. Twenty young adult rats were exposed to 300 ppm of styrene, and 15 littermate control rats were sham-exposed in a similar exposure chamber with air circulation. The rats were exposed for 6 h a day 5 d a week for up to 11 weeks. The motor conduction velocity of the tail nerve was measured from stimulation with a bipolar needle electrode at the root of the tail and from the recording of a coaxial needle electrode in the tail muscle at a distance of 12 to

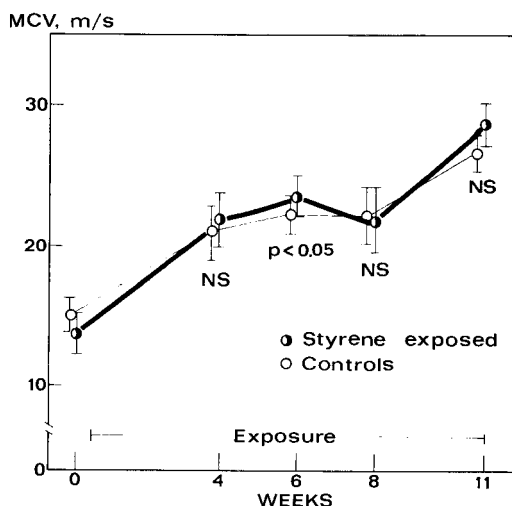


Fig. 1. The motor conduction velocity of the tail nerve of 20 young adult rats exposed to styrene and that of 15 littermate control rats.

13 cm from the stimulating electrode. A Disa electromyograph was used.

After six weeks of exposure to styrene the motor conduction velocity of the tail nerve was higher in the exposed rats than in the controls (fig. 1). This change was, however, transient, since in the later measurements, performed 8 and 11 weeks after the beginning of exposure, no difference could be detected between exposed and control animals. The question can be raised therefore of whether a transient increase in nerve conduction velocity might be indicative of beginning neurotoxicity. In addition there is the question of whether long-term exposure can induce real neuropathy or if adaptation occurs in the peripheral nerves. Central nervous involvement seems to be the first to appear within the nervous system.

REFERENCES

1. HÄRKÖNEN, H. Relationship of symptoms to occupational styrene exposure and to the findings of electroencephalographic and psychological examinations. *Int. arch. occup. environ. health* 40 (1977) 231—239.

2. SAVOLAINEN, H. and PFÄFFLI, P. Effects of chronic styrene inhalation on rat brain protein metabolism. *Acta neuropathol.* (Berlin) 40 (1977) 237—241.
3. SEPPÄLÄINEN, A. M. and HÄRKÖNEN, H. Neurophysiological findings among workers occupationally exposed to styrene. *Scand. j. work environ. & health* 2 (1976) 140—146.

QUESTIONS AND ANSWERS

Questions to Dr. Seppäläinen

- Dr. Hernberg: How do you explain that the conduction velocities increased so sharply also in the control group?
- Dr. Seppäläinen: The rats were young adults, so partly the increase may depend on age. Temperature of the environment may also be reflected, but both the exposed and control animals were studied on the same day in the same environment, so the comparison between them is justified.
- Dr. Rosén: Is there a possibility of remaining acute effects of styrene as an explanation for the increased occurrence of EEG abnormalities in styrene exposed subjects? Perhaps styrene influenced the level of wakefulness and therefore increased the amount of theta activity.
- Dr. Seppäläinen: There was always a pause of at least 16 hours between the last occupational exposure to styrene and the registration of the EEG. Although, as we have heard here, styrene remains in part in the body, we can assume that at the time of the investigation the styrene left in the body represents an equilibrium stage usual to the worker and thus does not cause any acute effects, either in the level of wakefulness or in other EEG parameters.
- Dr. Rosén: Have you considered looking at sensory neurographic parameters in your animal exposure experiments? From our results on humans we think that sensory neurons might be more sensitive to styrene effects than motor neurons.
- Dr. Seppäläinen: I have not performed measurements of sensory conduction velocities in rats, because an alert rat cannot be immobilized so that sensory nerve action potentials could be reliably measured. If feasible, sensory nerve studies could add to our knowledge on the neurotoxic effects of styrene.