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NEUROBEHAVIORAL EFFECTS OF EXPERIMENTAL EXPOSURE TO TOLUENE, XYLENE AND THEIR MIXTURE

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Abstract. The effects of experimental exposure to toluene (100 ppm), xylene (100 ppm) and their mixture (50 ppm of toluene and 50 ppm of xylene) on CNS functions were studied in 10 male volunteers aged 22—35. Changes in CNS functions were measured by means of nine psychological tests. Acute exposure to xylene produced the most adverse effect on simple reaction time SRT and choice reaction time ChRT. Exposure to toluene affected only the memory test performance. The effect of combined exposure appeared to be weaker than the effect of exposure to xylene alone but stronger than the effect of exposure to toluene.

INTRODUCTION

Organic solvents belong to the group of substances widely applied in industry, agriculture and household (8) and an adverse effect of exposure to these compounds has become a vital problem for occupational health service.

Numerous studies prove that exposure to organic solvents affects chiefly the central nervous system and, according to many findings, neurobehavioral tests play an important role in early detection of negative changes in CNS functions (2, 3).

According to Gamberale (2). "no interactional effects of the non-additive type on behavioral performance have been found for combined exposure to two solvents or for the combination of exposure to one solvent and the intake of alcohol or pharmaceuticals". (p.66). Occupational exposure is usually a combined one and, therefore, the problem of effects of such exposure seems to require further studies. An additio-

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nal stimulus for these studies are the results obtained in animal experiments carried out at the Nofer Institute of Occupational Medicine in Lodz, which revealed that the effect of combined exposure to toluene and xylene is more than additive (6). In view of the fact, that the former experiments had been carried out on animals exposed to highly concentrated solvents, it seemed justified to find out whether the effects of exposure to toluene-xylene mixture would be similar in humans exposed to concentrations close to those occuring in working environment.

MATERIALS AND METHODS

Subjects. Ten male volunteers aged 22—35 years were recruited mainly from the Institute's staff. All volunteers were subjected to medical examination including a clinical examination and hematological screening. The acceptance of the experiment's program and the levels of exposure was given by the Local Ethical Committee. In addition, all volunteers were informed in detail about the conditions of the experiment and finally each subject signed his consent for taking part in the experiment.

Exposure chamber. The exposure sessions were conducted in a chamber described in detail in a paper by Jakubowski and Wieczorek (4). The temperature and humidity were kept at a stable level. The concentration of the solvents' vapours was controlled by means of gas-chromatography and infra-red spectrophotometry.

Experimental design. The subjects were exposed to toluene, xylene and their mixture at a constant concentration of 100 ppm of toluene (376 mg/m^3), 100 ppm of xylene (434 mg/m^3) and 50 ppm of toluene with 50 ppm of xylene as a mixture. Each exposure session lasted 4 hours. The subjects were exposed in pairs to avoid a feeling of isolation. Each pair participated in four exposure sessions: to toluene, xylene, toluene-xylene mixture and control, with an interval of 7 days between each session. Within this pattern each volunteer played the role of control subject for himself. The sequence of particular kinds of exposure for each pair was random. The subjects were unaware to which chemical(s) they were exposed in particular sessions. Vapours of terpon compounds were used to mask the odour of the solvents. About one week prior to the first exposure day each pair attended a training session during which they had to perform the tests battery twice. The session timetable is presented in Table 1. Psychological tests were repeated three times and blood samples were taken four times during every session.

Table 1. Timetable

7.30 — breakfast
8.00 — pre-exposure testing outside the chamber (1)
8.45 — medical examination and drawing first blood sample
9.00 — entry into the chamber; begining of exposure
10.00 — performance testing (2)
10.55 — drawing second blood sample
12.00 — performance testing (3)
12.55 — drawing third blood sample
13.00 — end of exposure; leaving the chamber
13.15 — drawing fourth blood sample followed by medical examination

TABLE 2. Battery of tests

Name of test	Function
1. Sperling's test	memory
2. Stroop's test	interference of cognitive processes
3. Sternberg's test	cognitive processes
4. Flanagan's test	motor-visual coordination
5. Aiming	speed and precision of hand movements
6. Simple reaction time	psychomotor efficiency
7. Choice reaction time	psychomotor efficiency
8. Santa Ana	psychomotor efficiency
9. Profile of Mood State	mood

Psychological tests. The battery consisted of the tests presented in Table 2. The memory was measured by means of a technique which was used by Sperling in testing the iconic memory (7). A table with nine letters was presented on a screen for five seconds. After 5 sec. (1st version) and 10 sec. (2nd version) intervals the table without letters was displayed and the subjects were supposed to remember a letter which was situated in the marked place. Each version of the test consisted of ten tasks. Three results were computed for each subject: the number of correctly remembered letters in version I, in version II and difference between the results obtained in both versions. The second test was a computerized version of Stroop's test (11). Two groups of words were presented: names of colours (red, blue, green, brown and violet) and some other words. The colours' names were printed using either congruent or non-congruent colours. The subjects had to press a key on a keyboard when the name of colour was displayed. There were 60 items presented in random order. Mean reaction time for congruent items was measured. The difference between the mean times was a third result.

The third test was constructed according to additive factor methodology by Sternberg (10). We used indentification task version (9). Two sets of letters were displayed at the same time and the subjects had to press the key if the sets were identified as identical (positive item). There were 60 items: 40% negative and 60% positive ones. The sets

were differentiated according to the number of letters (set-size factor), the position or second element of item (rotation factor) and the masking or clear background (stimulus quality factor). Manipulation with the afore-mentioned factors affects the duration of mental operations engaged in information processing. The stimulus quality factor affects encoding operation and the rotation and set-size factors affect the comparative operation (10).

To measure motor-visual coordination Test 15 from Flanagen Aptitude Classification Tests was used (1). The next test applied was choice reaction time. Two small lights, green and red, were shown to the subjects. Their task was to press the button as soon as possible whenever the red signal appeared. There were 30 red and 30 green signals appearing in random order, at 1—10 sec. intervals. The rest of the tests has been taken from Neurobehavioral Core Test Battery recommended by WHO experts to measure effects of exposure to neurotoxicants.

RESULTS

Blood solvent concentrations were determined from blood samples collected at 0, 115, 235 and 245 minutes after beginning of exposure. Changes in solvent concentrations as a function of duration of exposure are presented in Fig. 1.

Because of small number of subjects the results of experiment were analyzed with the Friedman analysis of variance by ranks (SPSS program). Only performance of three tests appeared to be a sensitive tool to measure acute exposure to solvents used in experiment: Sperling Test (2nd version), SRT and ChRT.

The results of memory test are shown in Fig. 2. In the case of exposure to toluene there is a statistically significant relationship between number of errors and time of exposure ($p < 001$) as compared to control performance. This relationship is not linear. After one hour of exposure there was an improvement in performance of this test (the number of errors decreased) but after three hours of exposure performance returned to the preexposure level. No effect of exposure to xylene and toluene-xylene mixture was noted. The results of simple reaction time (SRT), which are presented in Fig. 3, revealed that only exposure to xylene significantly affected performance of this test ($p < .001$). Prolongation of simple reaction time depending on the time of exposure could be observed. The profile of changes for percent of choice reaction time (ChRT) is presented in Fig. 4. Exposure to xylene and toluene-xylene mixture induced a significant deterioration in performance of this test ($p \leq .001$ and $p \geq .05$, respectively).

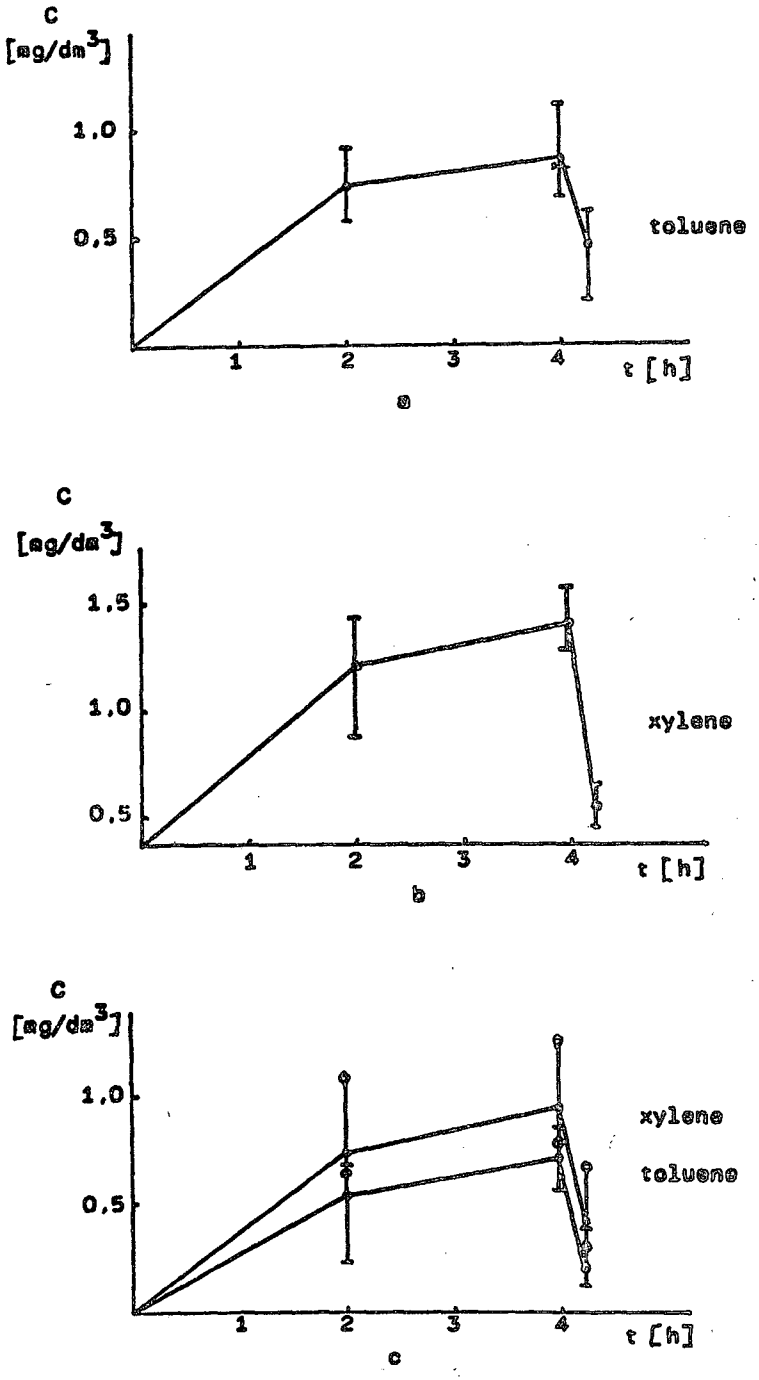

Fig. 1. Blood concentration of solvents (mean and range) as a function of exposure duration to toluene (a), xylene (b) and their mixture (c).

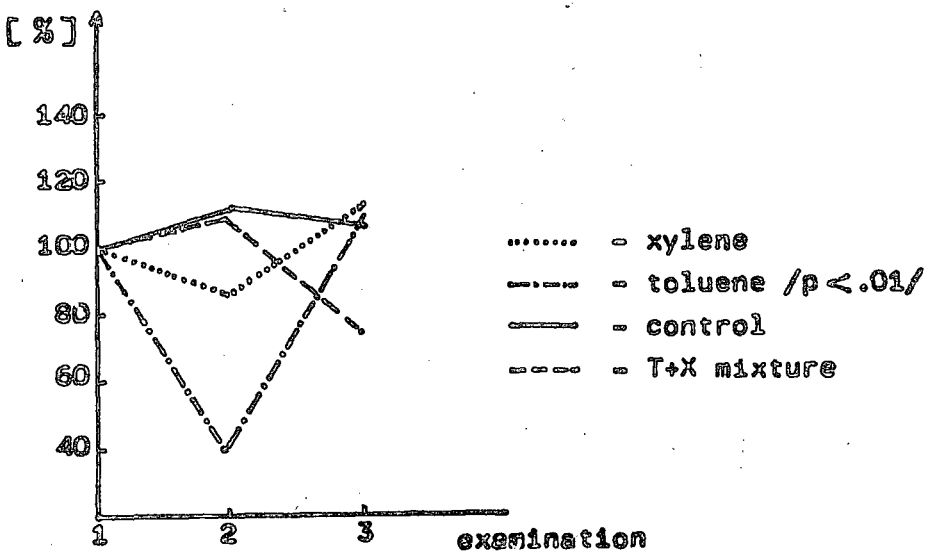

Fig. 2. Mean performance level on Sperling's test. Differences between pre-exposure level of performance and subsequent measurements during the various exposure conditions.

DISCUSSION

The study was designed to verify a hypothesis of more than additive effect of exposure to a mixture of toluene and xylene.

1. The results of our experiment did not confirm the findings from animal experiments (6). Exposure to xylene produced the most adverse effects (deterioration of performance) in SRT and ChRT. Exposure to toluene did not cause any significant-level decrease of reaction time. However, the effect of exposure to mixture was weaker than the effect of exposure to xylene, but stronger than to toluene.

2. Evident changes in central nervous system functions, measured by means of SRT and ChRT, caused by exposure to 100 ppm of xylene should be taken into account during setting MAC value that is to be obligatory in working environment.

3. It is difficult to interpret the results of Sperling's test. Most researches point to the negative effects of exposure to solvents on memory (5), which is contradictory to our results, although it may be due to using different methods for measurement of memory.

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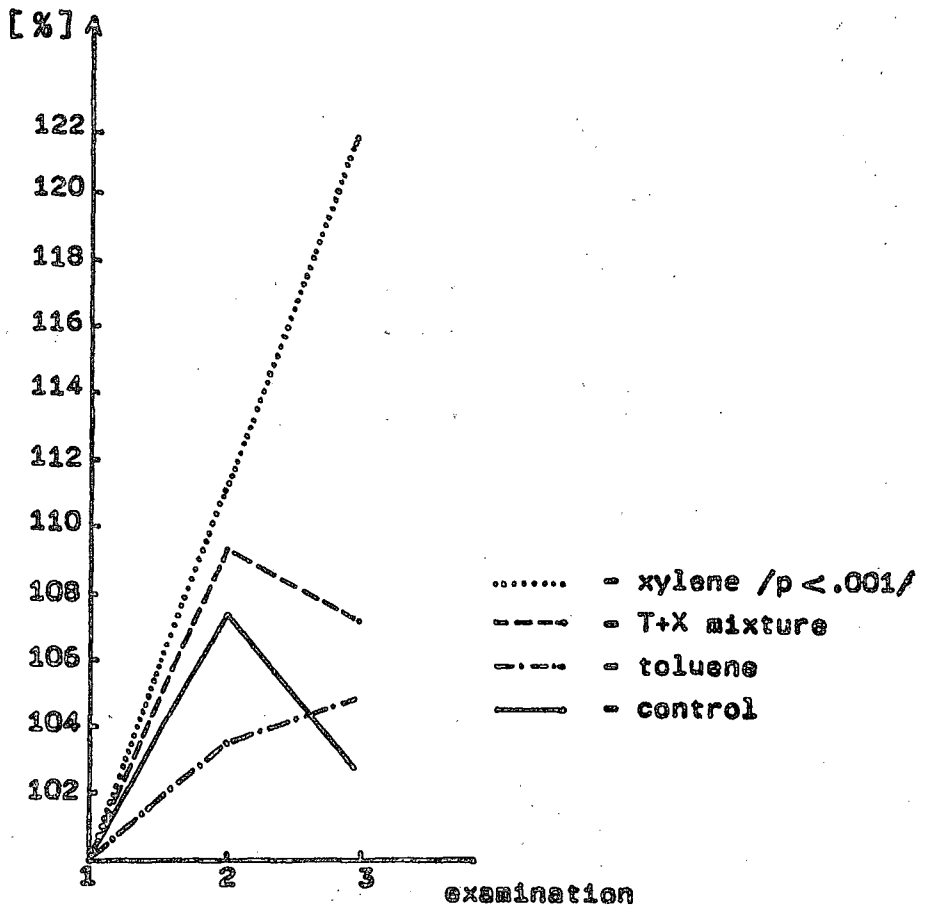

Fig. 3. Mean performance level on Simple reaction time. Differences between pre-exposure level of performance and subsequent measurements during the various exposure conditions.

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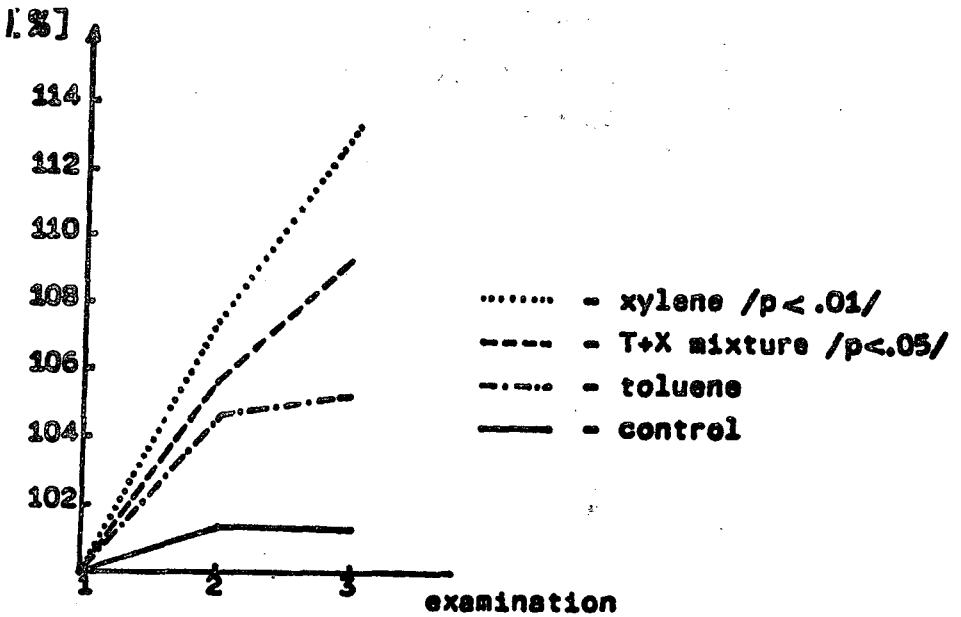

Fig. 4. Mean performance level on Choice reaction time. Differences between pre-exposure level of performance and subsequent measurements during the various exposure conditions.

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