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16. Abstract (Limit: 200 words)

The effects of trichloroethylene (79016) (TCE) on behavioral and cognitive performance were investigated. Nine volunteers were exposed for 8 hours per day for 3 days to 0.50, and 110 parts per million (ppm) of TCE; each exposure session was separated by a 4 day nonexposure period. Breath samples were taken at selected postexposure intervals for TCE and metabolite analysis. During the first and last hour of each exposure session, subjects completed complex reaction time, tachistoscopic perception, digit span, finger dexterity, flanagan coordination, and digit inspection tests. Subjective responses to exposure were also determined. The subjects reported various symptoms including headache, dizziness, and eye, nose and throat irritation. TCE exposure significantly affected performance only on the flanagan coordination test. Sources of variability on the other tests included learning effects, time of day, and subject. Results of breath analyses were not evaluated. The authors note these findings do not substantiate the positive results in a previous study of subjects exposed to 110ppm of TCE. They suggest that the discrepancy could be due to statistical methods, control of exposure concentrations, and exposure design.

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EFFECTS OF TRICHLOROETHYLENE ON BEHAVIORAL PERFORMANCE CAPABILITIES

EFFECTS OF TRICHLOROETHYLENE ON BEHAVIORAL PERFORMANCE CAPABILITIES

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To protect American workmen from the toxic effects of trichloroethylene (TCE) a Threshold Limit Value (TLV) of 100 ppm has been established [1,2]. Recently the adequacy of this workplace standard has been questioned [3,4]. In 1971, Salvini, Binaschi and Riva reported degradation of behavioral performance in six university students exposed to TCE 110 ppm for a single eight-hour work day [3]. As a result of "statistically very significant" performance decrements in complex reaction time, tachistoscopic perception, finger dexterity, and the Wechsler memory test, these authors concluded that a TLV of 110 ppm "appears to be very close to the average concentration capable of interfering with psychophysiological efficiency".

To investigate these TCE-induced behavioral performance decrements, the study described below was undertaken.

EXPERIMENTAL METHOD

One of the authors visited the laboratory of Salvini, Binaschi and Riva at the Institute of Preventive Medicine for Workers and Applied Psychology, University of Pavia, Italy, to study the testing equipment and the methodology described by the Italian scientists [3,5]. Then an expanded version of the Salvini experiment was performed in which two TCE vapor concentrations were investigated instead of one. Three female and six male volunteers were exposed in groups of three in a controlled-environment chamber to TCE vapor concentrations of 0, 50, and 110 ppm for eight hours. Each exposure day consisted

of a 4-hour exposure in the chamber, a $1\frac{1}{2}$-hour lunch period outside the exposure chamber followed by an additional 4 hours of exposure in the chamber. Behavioral performance tests were carried out twice each exposure day. Four non-exposure days elapsed between each TCE exposure.

Volunteer Subjects:

The three females, designated Group I, were 26, 34 and 42 years of age and were all housewives. Group II consisted of males of ages 19, 22 and 29. One was a physician, while the other two were temporarily unemployed. Group III consisted of males ages 22, 23 and 28, all temporarily unemployed.

This investigation was performed with strict adherence to the ethical and technical requirements for human inhalation experimentation previously detailed, which included obtaining the informed consent of each subject after the objectives of the study and the nature of the procedure had been fully explained [6]

Exposure Schedule:

Table I details the exposure sequences for this series of experiments. In addition to the TCE vapor exposure of 110 ppm investigated by Salvini, et al, each group was exposed to 50 ppm, expanding the data base so that a dose-response relationship could be sought. Neither the subjects nor the investigators giving the behavioral tests were informed as to the TCE vapor concentration on any given day.

TABLE I

ACUTE 8-HOUR EXPOSURE TO TRICHLOROETHYLENE VAPOR

Exposure Day	Session	Vapor Exposure, ppm (Mean ± S. D.)		
		Group I	Group II	Group III
1	4-hr Morning	0	110 ± 2	51 ± 4
	4-hr Afternoon	0	112 ± 3	49 ± 1
2	4-hr Morning	113 ± 4	56 ± 4	0
	4-hr Afternoon	114 ± 2	50 ± 1	0
3	4-hr Morning	49 ± 2	0	110 ± 2
	4-hr Afternoon	49 ± 2	0	110 ± 2

Exposure Chamber:

Exposures to TCE were conducted in a controlled environment room 20 ft x 20 ft x 8 ft in size, which contained a 5 ft x 4 ft x 8 ft toilet facility and a 4 ft x 5 ft x $6\frac{1}{2}$ ft audiometric booth, both of which were ventilated with exposure chamber air. Exhaust air flow was approximately 500 cu ft/min, creating a slight negative pressure within the chamber. The ambient temperature in the facility was maintained at 72° - 74° F, while the relative humidity ranged between 45 - 55%.

Liquid TCE was pumped at a constant rate into a heated flask. A stream of air flowing through the flask swept the TCE vapor into the return air duct of the chamber. The proportion of fresh air used by the system was varied along with the TCE pumping rate to achieve vapor concentration control.

Analysis of Exposure Chamber Atmosphere:

The TCE used in these experiments was 99.9% pure. The vapor concentration in the chamber atmosphere was continuously recorded by an infrared spectrometer equipped with a variable path-length gas cell set at 5.25 meters. The gas cell was continuously flushed with air drawn from the test facility through a $\frac{1}{4}$-inch diameter polyethylene tubing. Transmittance at 11.74μ was monitored every second by an on-line Digital PDP-12 computer, which recorded the mean vapor concentration for each 30-second time interval of exposure and the time-weighted-average exposure from the beginning of each session. A gas chromatograph equipped with a hydrogen flame ionization

detector and an automatic sequential sampler provided a second independent method for analyzing the exposure chamber atmosphere. Calibration standards of TCE in pure air were prepared in saran bags and analyzed before and hourly by both instruments during each daily exposure.

Breath Sample Collection and TCE Analysis:

Alveolar breath samples were obtained from each subject prior to exposure and at the following post-exposure times: 1 and 30 minutes, 1, 2, 4 and 16 hours [7]. Samples obtained prior to exposure and 1 and 30 minutes post-exposure were collected in saran bags. The remaining samples were collected in 35-ml glass tubes fitted with screw caps containing saran liners. One of the caps had a pre-drilled hole through which a gas sample could be withdrawn. The subjects flushed the tube three times, then after holding the fourth breath for 30 seconds, exhaled and capped the tube while finishing the exhalation.

A Varian Aerograph Model 2700 gas chromatograph equipped with a hydrogen flame ionization detector was used to determine TCE in the breath samples. The gas chromatograph (GC) was fitted with a stainless steel column, 3 ft x 1/8 in, packed with 25% Apiezon L on Chromosorb W, AW, 45/60 mesh. The column was preconditioned at 220°C overnight prior to its use. The operating conditions of the GC were as follows: carrier gas (helium) flow rate, 40 ml/min; column temperature, 105°C; injection port, 210°C; and detector 250°C. Standards at five concentrations to bracket the unknown levels were prepared with air as the diluent. One-ml aliquots were

injected in duplicate and the concentration of TCE in unknowns was obtained by direct comparison of peak heights to those of the standards.

Medical Surveillance:

Each subject was given a comprehensive medical examination three days prior to the first day of exposure. This examination was repeated the day following each individual's last exposure. Each examination included a complete history and physical examination with the following laboratory studies: complete blood count, SMA-12 survey panel of clinical chemistries, urinalysis, 12-lead electrocardiogram, Orthorater visual performance profile (initial examination only) and a pregnancy test (initial examination on females only). Prior to each day's exposure, the subjects were given a repeat medical examination and were under continual surveillance by medical personnel while they were in the chamber. During all sessions spent in the environmental chamber, each subject's electrocardiogram (lead II) was continuously monitored by telemetry, and recorded at hourly intervals.

All subjects, when wearing glasses, had normal visual acuity. None of the female subjects was pregnant the day prior to her first TCE exposure.

Behavioral Performance Testing:

Behavioral tests were carried out twice each day while the subjects were in the chamber: first upon entering the chamber for the morning session and then $1\frac{1}{4}$ hour prior to leaving the chamber during the afternoon session. Total time required for each test session was 1 hour and 5 minutes. The six

tests used are described below in the order in which they were given. Because only one apparatus for each of the Salvini procedures was available, the three subjects exposed on any given day entered and exited the chamber at 15-minute intervals, and always in the same sequence.

Training for the test battery was carried out on the day prior to the first exposure. At that time each task was explained and one practice session was held.

Subjects were told that they would be exposed to TCE vapor, 110, 50 or 0 ppm, but they were not informed as to the vapor concentration on any given exposure day. Before starting the series of three exposures, they were encouraged to do their "best" on every task. They were given no feed-back on performance prior to the end of the exposures. Each test was always administered by the same individual.

As Salvini had done, all subjects exercised for 20 minutes at approximately 3 cal/min on Monark bicycle ergometers, midway through each session or twice per exposure day.

Complex Reaction Time:

The subject was seated 24 inches from a 16-inch square wooden panel containing one central neon lamp and six peripheral neon lamps radially disposed 3.9 inches apart (Figures 1, 2). On the rear of the panel was mounted a "bird chirp" auditory signal. The subject's responses to visual or auditory signals were via two hand-held push-button devices and two foot pedals. The

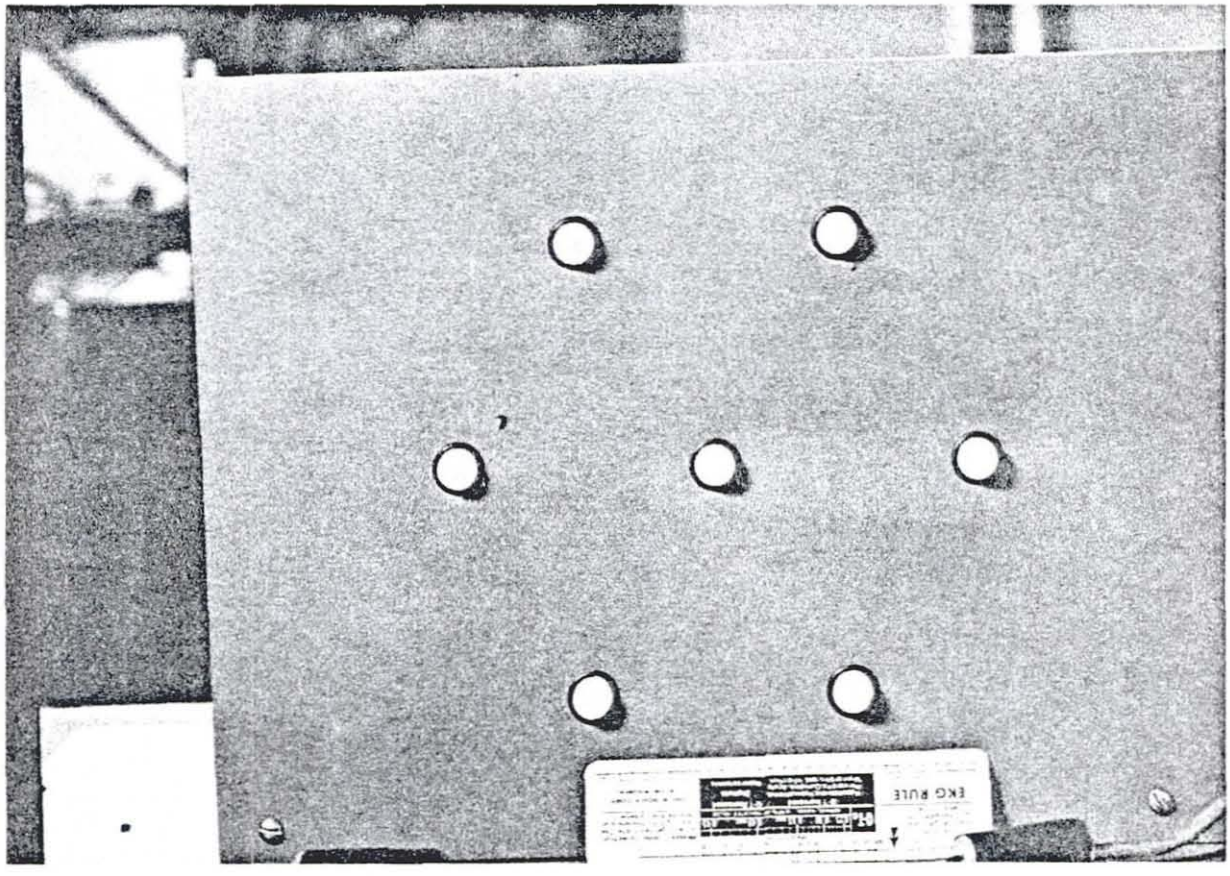

FIGURE 1

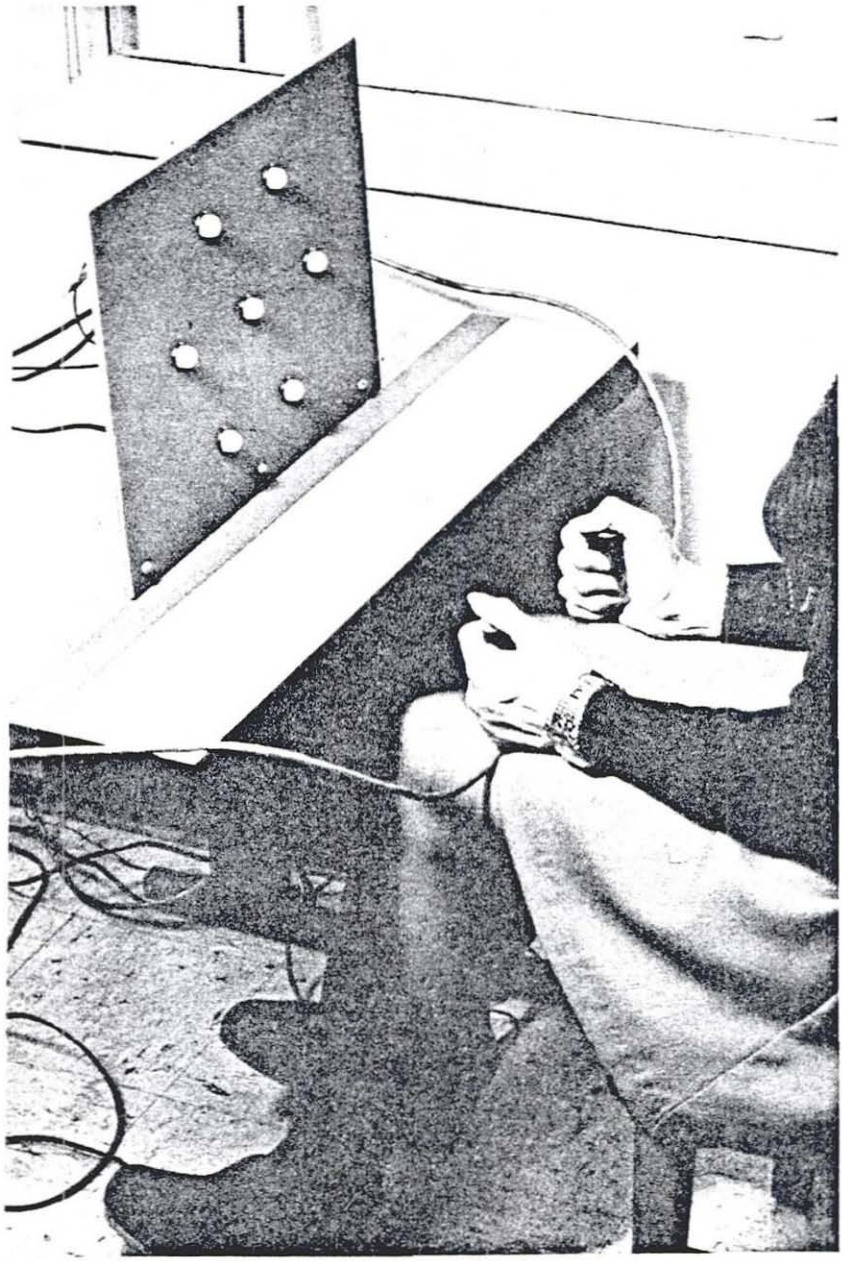

FIGURE 2

incident room illumination was 8-foot candles.

The task consisted of responding to 42 stimuli which were automatically and randomly presented with BRS-LVE solid-state programming equipment. Stimuli were 1/50 second in duration and were presented at the rate of one every 15 seconds. The total duration of this task, therefore, was $10\frac{1}{2}$ minutes. The subjects were instructed to respond as quickly as possible so that reaction time to each stimulus presented, incorrect responses and missed stimuli could be recorded. When the three lamps on the right side of the panel lit, the subject was instructed to press the hand-held push-button device with his left thumb; when the three lamps on the left side lit he pressed the hand-held push-button with his right thumb. He responded to the central light be depressing the right foot pedal and to the auditory signal by depressing the left foot pedal. Reaction time in milliseconds was registered by a Hunter Manufacturing Company Model 220 C Klock Counter (Figure 3).

Tachistoscopic Perception Test:

In this test the subject viewed a series of 13 slides projected onto a screen (Figure 4). Each image contained a large square subdivided into nine equal squares. In the smaller squares either 4, 5, or 6 black circles randomly appeared (one per square). The subject's task was to reproduce as accurately as possible the exact pattern of black circles he saw by drawing X's in the corresponding squares of an answer sheet. Stimuli were presented for 1/20 second by means of a Ralph Gerbrands Company Model 61168 Electronic Tachistoscopic Shutter with Timer and Kodak Custom Carousel 800 HC (low

FIGURE 3

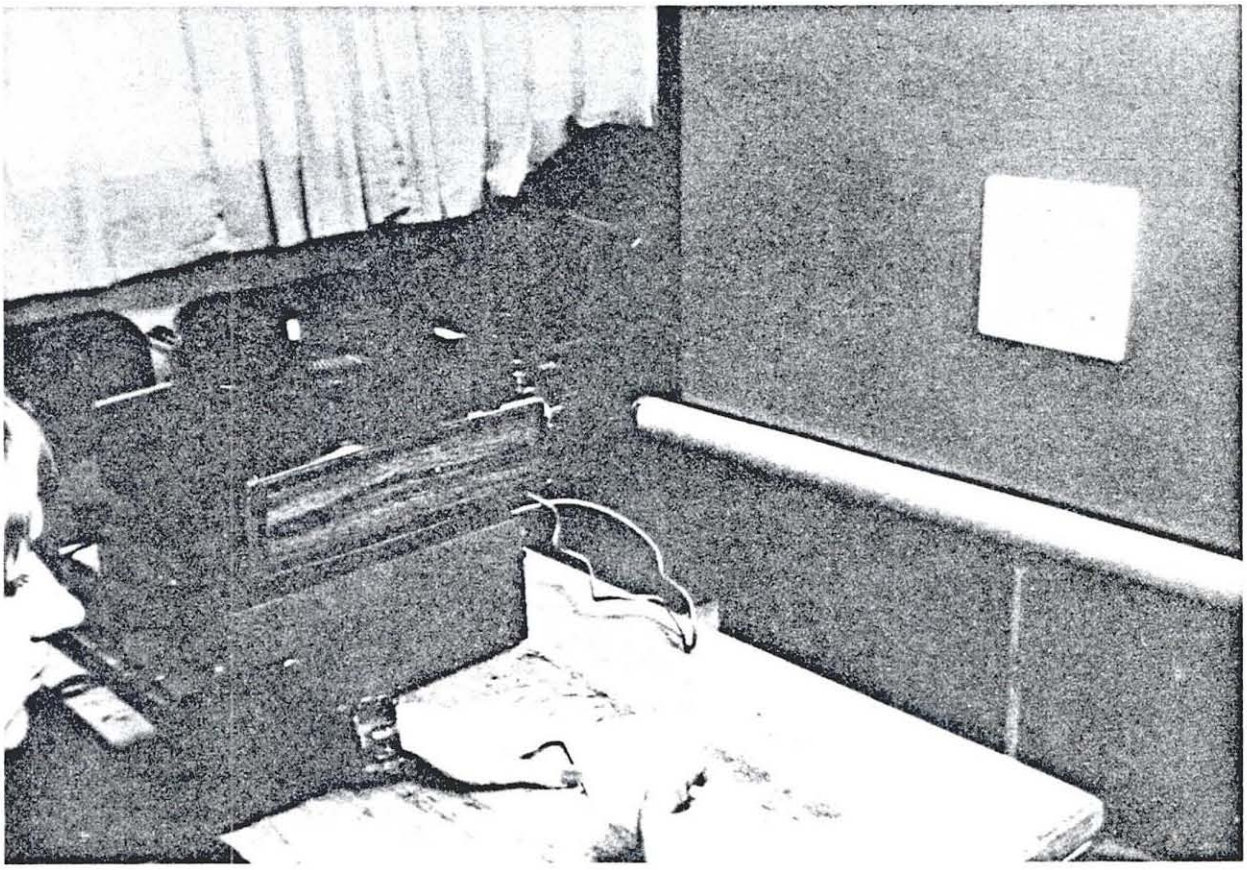

FIGURE 4

intensity) Projector. The projected image was 9 inches square and the viewing distance was 45 inches; the stimuli subtended a visual angle of 12°. The brightness of the test image at the screen was 500 foot candles. Room illumination was 40 foot candles at the screen.

Four slides contained four black circles, another four slides contained six black circles, and the remaining five slides contained five black circles all randomly placed within the nine inner squares. The 13 slides were rotated 90° to present a different randomly ordered group of slides for each test session.

The test was scored as follows: a one-point penalty was given for each black circle omitted and a $\frac{1}{2}$-point penalty was given for each transposition.

Digit Span Test:

Lists of successively increasing numbers of randomly generated digits were orally presented to subjects who were comfortably seated in the audiometric booth (Industrial Acoustics Company Model 401) located in the controlled-environment chamber (Figure 5). The subject's task was to repeat the number presented, first in a digits forward and then in a digits backward manner. The standardized instructions for the administration of this test were followed[8]. A different random order of digits was generated for each test session. The test score was the total number of digits correctly repeated forward plus the number correctly repeated backward.

FIGURE 5

Finger Dexterity Test:

The subject's task in this test was to place as many sets of three metal pins in small round holes as he could in 9 minutes. For the first three minutes the task was performed with the right hand, then for three minutes with the left hand and, finally, for three minutes with alternate hands. A board with 100 holes, each large enough to hold four pins, was placed in front of the subjects. The subject was instructed to pick up three pins at a time and fill as many of the holes as possible within the allotted time (Figures 6, 7), starting in the farthest corner opposite to his hand. The test score was the total number of holes filled with three pins in the allotted time. Incident desk top illumination was 110 foot candles. The test device was purchased from the Lafayette Instrument Company, Lafayette, Indiana.

Flanagan Coordination Test:

The Flanagan Coordination Test and the Digit Inspection Test were added to the test battery studied by Salvini so that the responses of the nine volunteers could be compared with those of other volunteers chronically exposed to TCE who had performed these two tests [9].

The Flanagan Aptitude Classification Test 7A, Coordination, published by Science Research Associates, Inc., 259 East Erie Street, Chicago, Illinois, is a paper-pencil test which requires a seated subject to trace a spiral pathway with a pencil (Figure 8). The standardized instructions for the administration of the test were followed. Forty seconds were allowed for

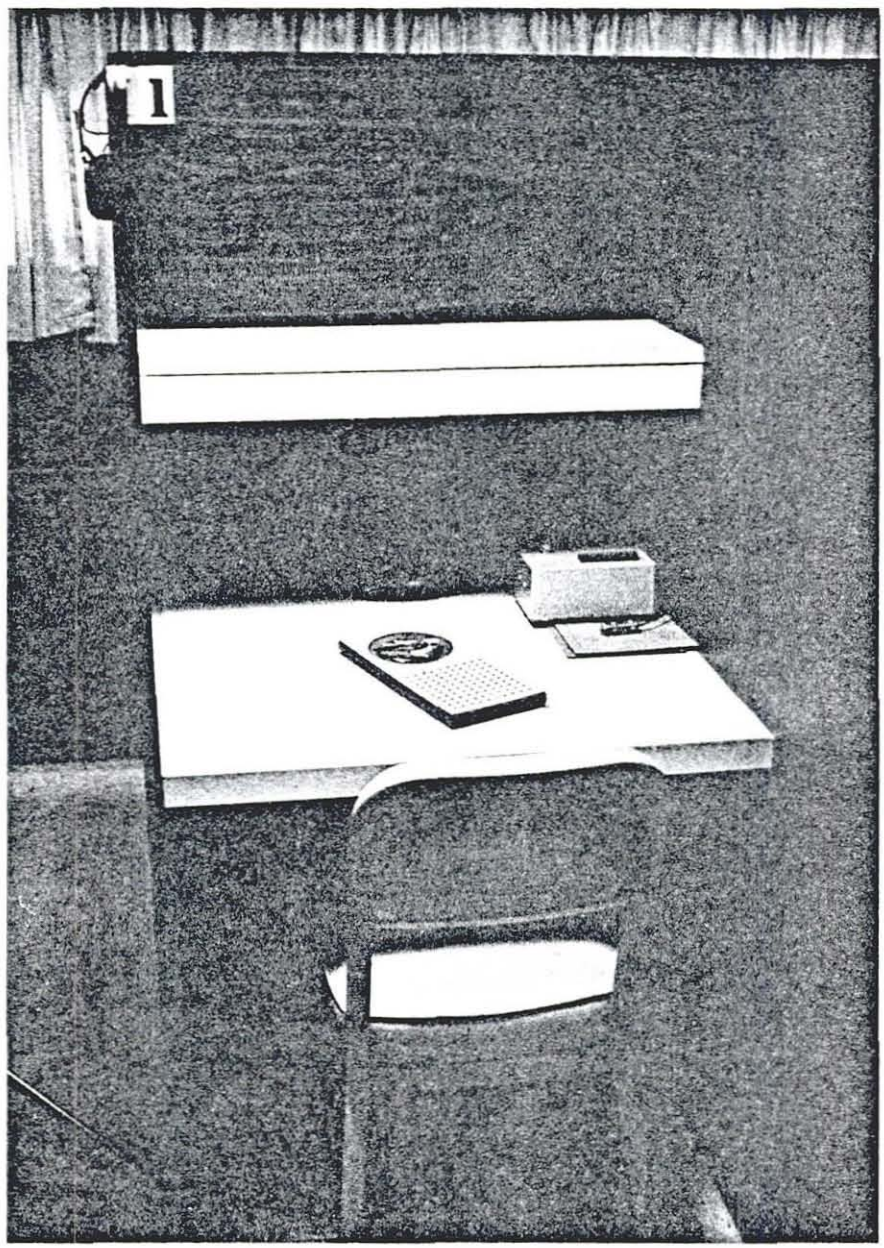

FIGURE 6

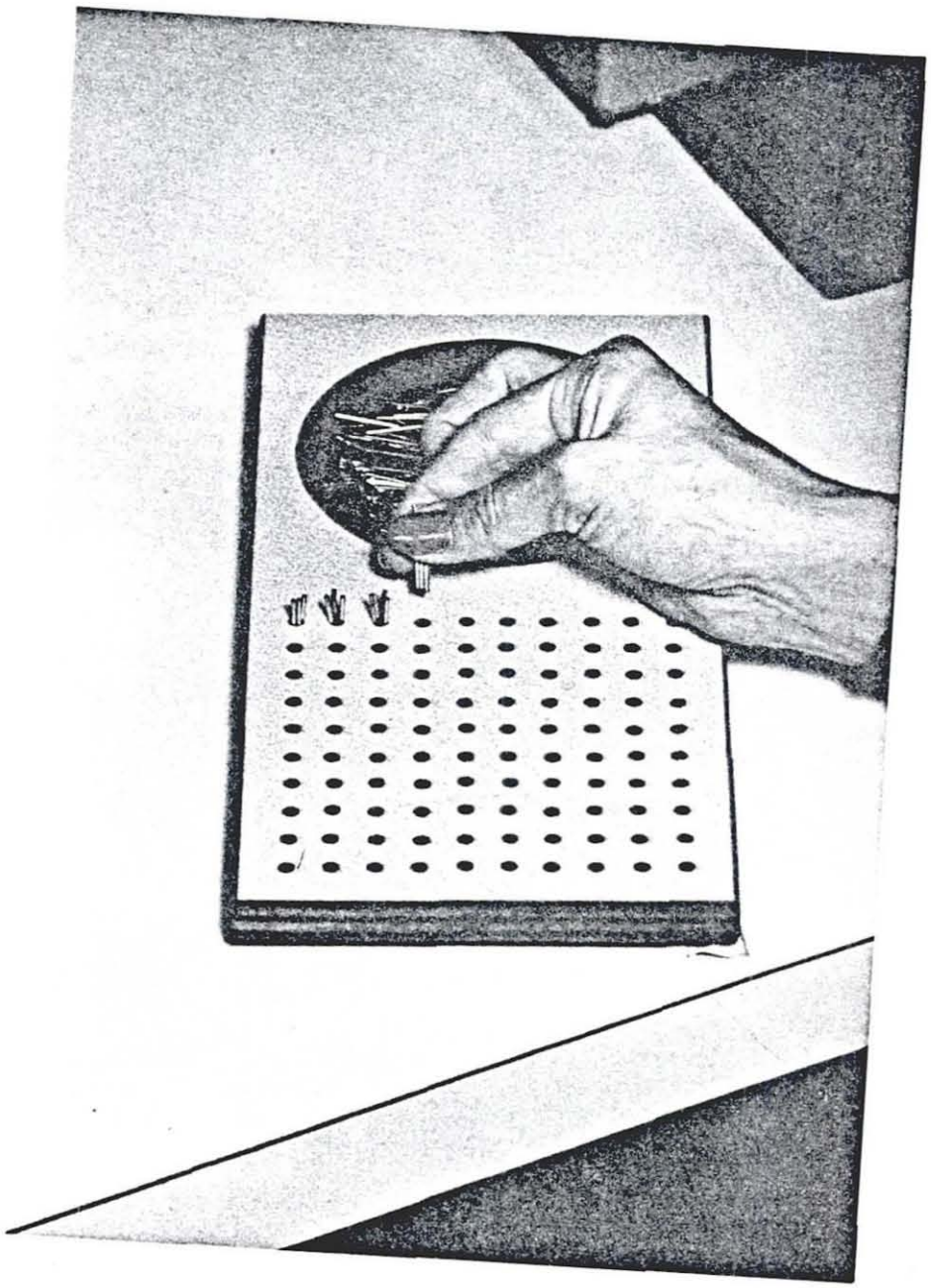

FIGURE 7

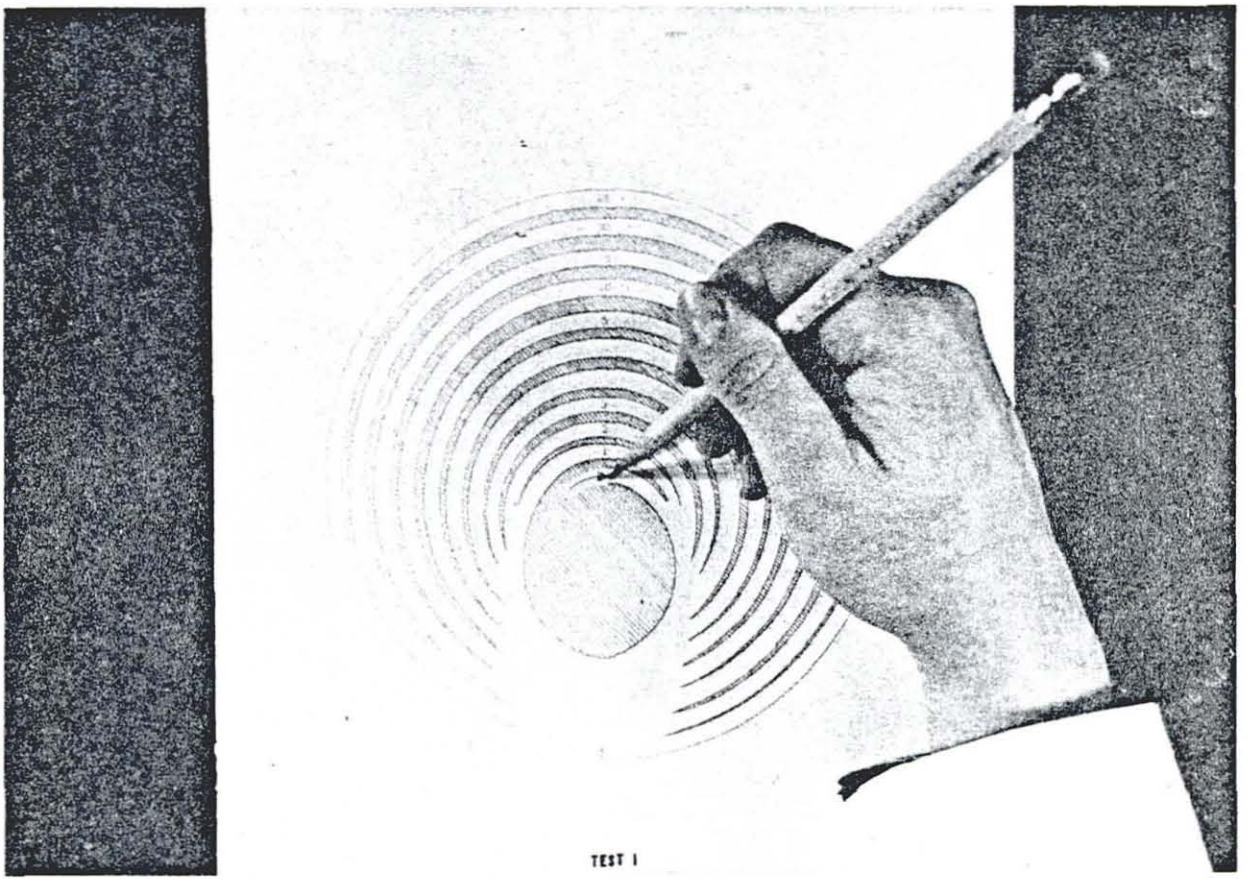

FIGURE 8

the completion of each of the six spirals. The first two spirals were practice tests while the last four were scored. The test score was a function of the distance traced minus the number of times the edges of the spiral pathway were touched with the pencil.

Digit Inspection Test:

This test was a measure of the speed with which a subject could detect the number "3" in rows of random numbers on an $8\frac{1}{2}$ x 11" page (Figure 9). The subject, while comfortably seated at a desk, was asked to inspect each row of numbers beginning at the top of the page and mark as many 3's as possible in two minutes. The subject's score was the total number of "3's" struck. A different page of random numbers was used each test session.

Subjective Responses:

All subjects were required to complete a subjective response form immediately after entering the chamber and hourly thereafter until four hours post-exposure. The form inquired as to the presence of headache; nausea; dizziness; abdominal pain; chest pain; eye, nose, throat irritation; and solvent odor (absent, mild, moderate or strong). The subjects were instructed to record any untoward response on this form.

RESULTS

The time-weighted average TCE vapor concentrations in the chamber for each four-hour session are listed in Table I. These concentrations were

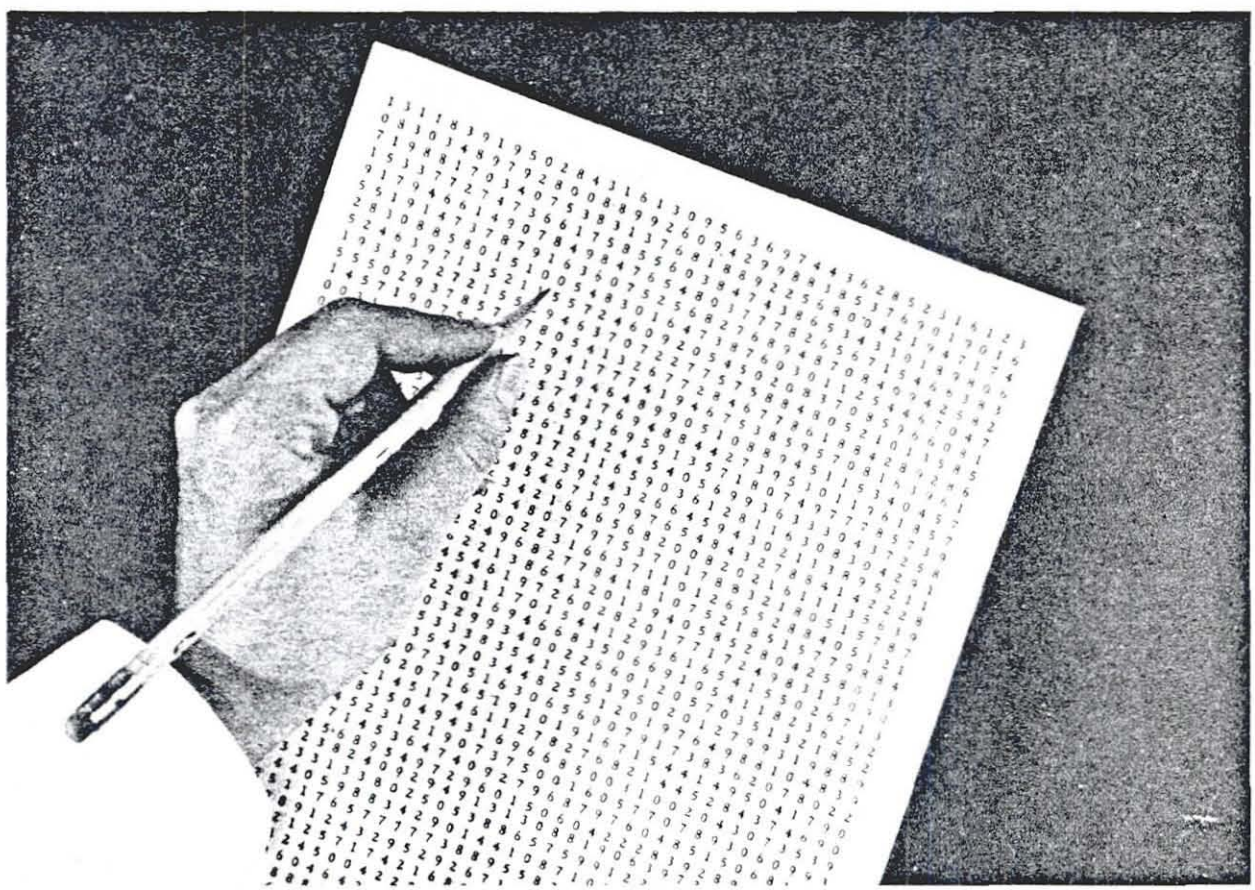

FIGURE 9

within $\pm$ 4% of that planned, with the exception of the second exposure of Group II, when the morning session averaged 12% above the planned 50 ppm concentration.

The post-exposure TCE breath decay curves are plotted in Figure 10. No TCE (detection limit of 0.01 ppm) was present in the pre-exposure breath samples.

Pre-exposure physical and medical examinations to determine the health of each subject prior to the series of exposures and prior to each individual exposure revealed no significant abnormalities. The physical and medical examinations conducted the day after the last exposure revealed no significant changes, indicating that all subjects had remained in good health. The subjective responses reported during the three separate days of exposure are summarized in Table II. An entry, "1/3 slight", in the headache row indicates that one of three subjects noted a slight headache some time during the exposure or in the first four hours thereafter. A dash indicates that no subject gave a positive response during any of the time periods.

Data Analysis:

The design of the Salvini experiment was such that an analysis of variance procedure was most appropriate to assess the significance of the variables which had the potential for influencing the six behavioral performance tests. These variables were: (1) the concentration of TCE vapor; (2) the day of the exposure sequence on which a test was performed; (3) the time

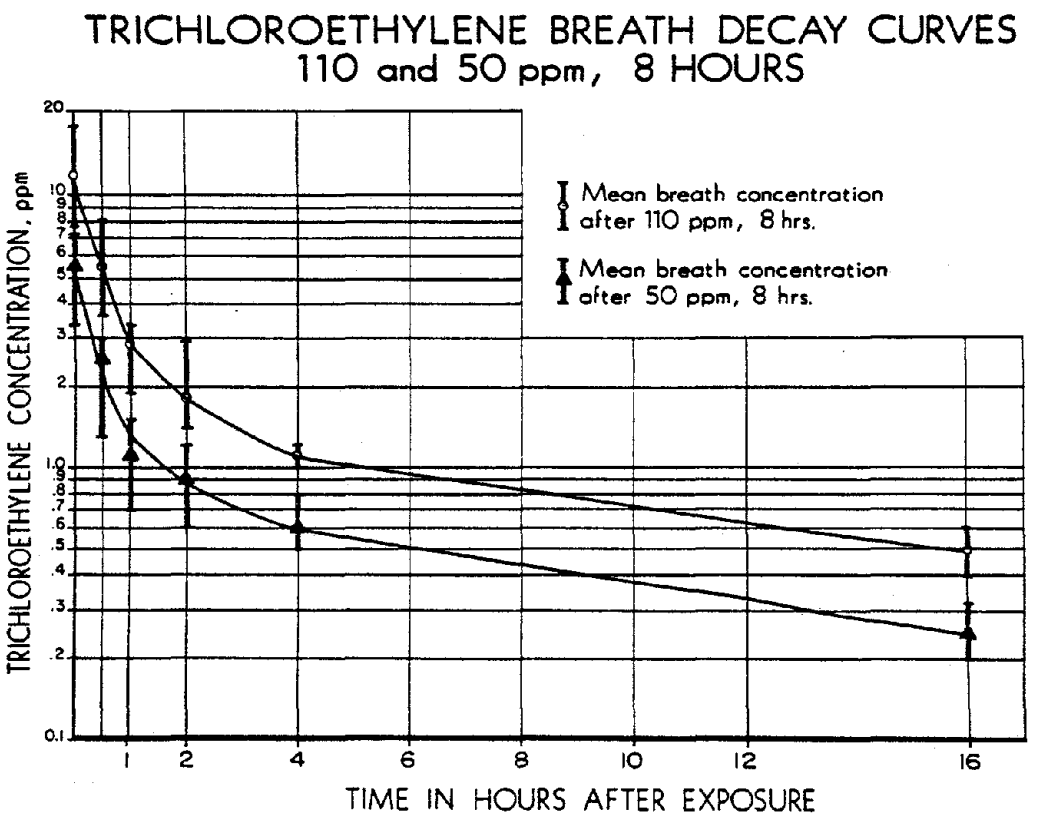
TRICHLOROETHYLENE BREATH DECAY CURVES
110 and 50 ppm, 8 HOURS
TRICHLOROETHYLENE CONCENTRATION, ppm
Mean breath concentration after 110 ppm, 8 hrs.
Mean breath concentration after 50 ppm, 8 hrs.
TIME IN HOURS AFTER EXPOSURE

FIGURE 10

TABLE II

SUBJECTIVE RESPONSES TO TRICHLOROETHYLENE VAPOR EXPOSURE

	Group I Exposure Sequence			Group II Exposure Sequence			Group III Exposure Sequence		
	0 ppm	110 ppm	50 ppm	110 ppm	50 ppm	0 ppm	50 ppm	0 ppm	110 ppm
Subjective Responses:									
Headache	2/2 slight	- -	- -	- -	- -	- -	- -	1/3 slight	1/3 slight
Nausea	- -	- -	- -	- -	- -	- -	1/3 slight	- -	1/3 slight
Dizziness	- -	- -	- -	- -	- -	- -	2/3 slight	1/3 slight	1/3 slight
Abdominal Pain	- -	- -	- -	- -	- -	- -	1/3 slight	- -	- -
Chest Pain	- -	- -	- -	- -	- -	- -	1/3 slight	- -	1/3 slight
Eye, Nose, and Throat Irritation	2/2 slight	- -	- -	- -	- -	- -	1/3 slight	2/3 slight	1/3 slight
Other Untoward Responses	- -	- -	- -	- -	- -	- -	2/3 drowsy	- -	2/3 drowsy
Odor	2/2 mild	3/3 strong to mild	2/3 moderate to mild	3/3 strong to mild	3/3 moderate to mild	- -	3/3 strong to mild	- -	3/3 strong to mild

of day the test was performed; (4) individual differences between the nine subjects in their ability to perform a test; (5) the differences in test performance ability between the three groups, and (6) combinations of interaction factors.

The analysis procedure for each of the behavioral tests was to construct analysis of variance tables for each group of three subjects. Next, a final analysis of variance table was constructed so that variation attributable to groups, subjects in groups, TCE vapor concentration, day sequence, residual interactions, am - pm effect, and finally, the interactions of am - pm effect with groups, TCE vapor concentration, day sequence and residual interactions could be assessed. Considering each of the three groups separately, the TCE vapor concentration source is confounded (inseparable) with the day sequence source. This means the differential effects due to TCE vapor concentration and day sequence can not be independently examined in each group. By nature of the experimental design for the three groups as a composite, the variation due to TCE vapor concentration and day sequence can be tested for significance. Assuming negligible interactions with groups, F-ratios in each analysis of variance table are used to judge whether the indicated source is a significant or non-significant source of variation.

Day sequence represents differences between day 1, day 2 and day 3. Performance of some of the behavioral tests improves with practice or training, and day sequence reflects this learning effect. The source TCE vapor concentration measures differential effects due to the three vapor

concentrations. Each of the TCE vapor concentration and day sequence sources is represented by 2 degrees of freedom in each analysis of variance table. The TCE x day sequence interaction, reflecting pattern changes in TCE mean responses across day 1, 2, and 3, would normally be represented by a 4 degree of freedom source of variation. However, this particular interaction is mathematically separated into two parts of 2 degrees of freedom each. Due to the design of the experiment, one part is confounded with the three groups while the other part, unconfounded with groups, is labeled residual interactions. Interactions involving groups with TCE or day sequence were presumed to be negligible. The TCE vapor concentration and day sequence sources are assessed appropriately by the residual (1) mean square in each analysis of variance table.

The am - pm source represents differential responses measured between the morning and afternoon. Since this is a within a day effect it can be considered to measure the influence of fatigue. Interactions involving am - pm depict am - pm pattern changes associated with changes in the indicated factors. For example, if the day sequence x am - pm interaction is significant, as it was in the inspection test, this indicates that the relation of the am response to the pm response is not the same for each of days 1, 2 and 3. Thus, the analysis of variance table summarizes the relative influence of the many sources of variation.

The mean test scores for each of the behavioral tests are presented

in Figures 11 - 16. The white circles designate the am mean scores while the black circles represent the pm scores.

Complex Reaction Time:

The mean complex reaction times for the 42 stimuli comprising each test are presented in Figure 11. In those instances in which the subject failed to respond to a stimulus, the average reaction time for the remainder of the stimuli was inserted so that a balanced set of data could be subjected to statistical analysis.

Trichloroethylene exposure did not appear to be a significant factor in the number of errors commited or missed stimuli. The number of errors recorded for the nine subjects were as follows: TCE 0 ppm, 16 errors; TCE 50 ppm, 17 errors; and TCE 110 ppm, 16 errors. The number of missed signals were as follows: TCE 0 ppm, 7; TCE 50 ppm, 1; and TCE 110 ppm, 6.

Table III presents the final analysis of variance for the complex reaction time response. Here are indicated the significant effects for subjects in groups and the subject x am - pm x session in group interaction. The interaction indicates that the am - pm response pattern across the three days is not the same for all subjects and this is seen in Figure 11. Effects due to TCE vapor concentration, day sequence, and am - pm effect are not judged significant.

Figure 11

Complex Reaction Time Mean Responses and 95% Confidence Intervals

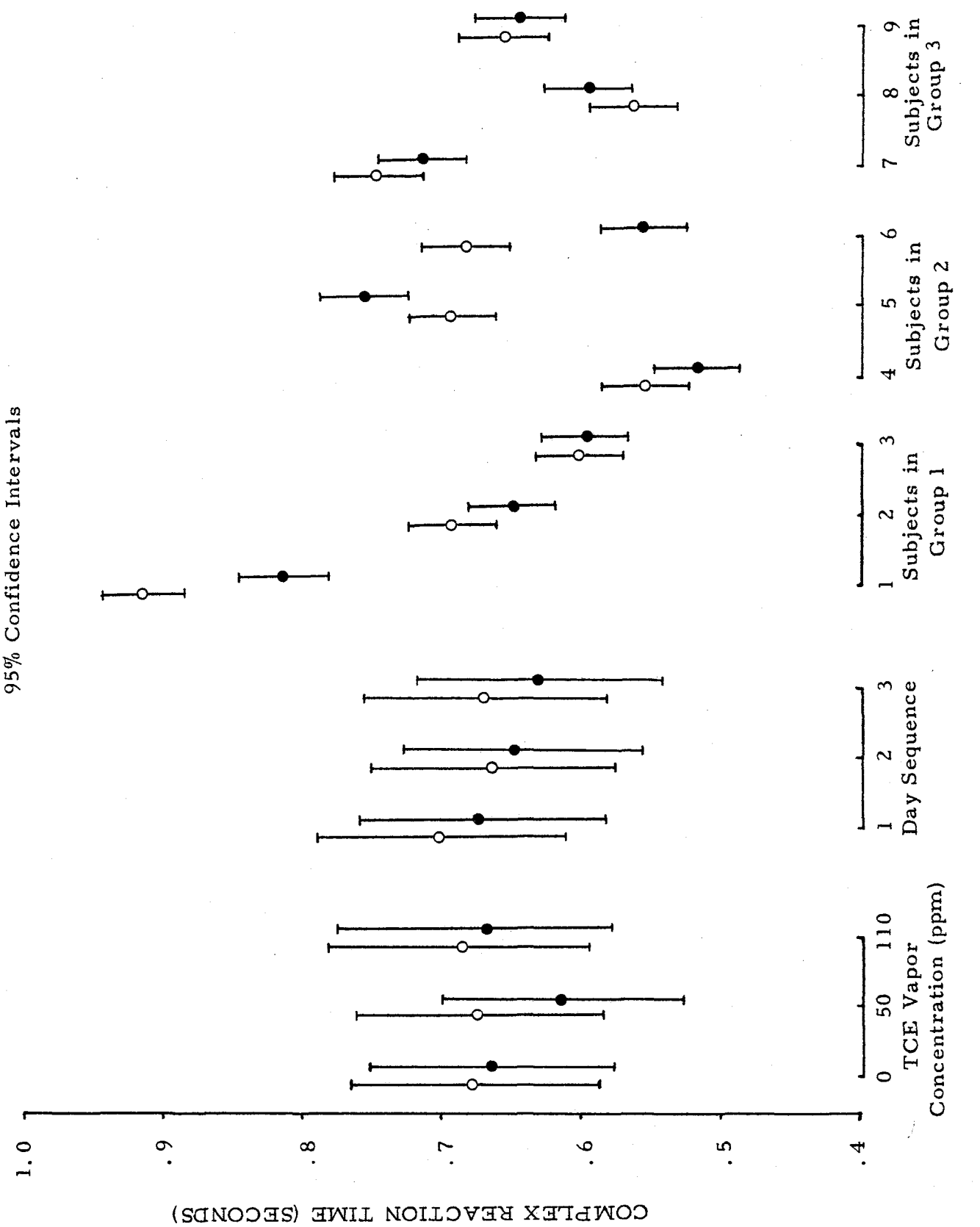

TABLE III
FINAL ANALYSIS OF VARIANCE FOR COMPLEX REACTION TIME

Source	DF	Sum of Squares	Mean Square	F Ratio	
Groups	2	2.8388	1.4194	.5015	NS
Subjects in Groups	6	16.9807	2.8301	86.5474	P<.001
Day Sequence	2	.5772	.2886	.4781	NS
TCE	2	.4415	.2207	.3656	NS
Residual Interactions	2	.0401	.0200	.0332	NS
Residual (1)	12	7.2436	.6036	18.4587	
am pm	1	.5027	.5027	1.9576	NS
am pm x Group	2	.2117	.1059	.4123	NS
Day Sequence x am pm	2	.0399	.0200	.1938	NS
TCE x am pm	2	.2587	.1294	1.2539	NS
Residual Interaction x am pm	2	.3263	.1632	1.5814	NS
Subject x am pm in Group	6	1.5410	.2568	7.8532	P<.001
Subject x am pm x Session in Group	12	1.2386	.1032	3.1559	
Residual (2)	2214	72.4283	.0327		

Tachistoscopic Perception Test:

The mean performance scores are presented in Figure 12. Analysis of variance (Table IV) indicates that the only significant source of variation is the subjects in groups. This variability among subjects is evident upon inspection of Figure 12. Variation among subjects is also significant within each of the three groups (analysis not presented). TCE vapor concentration, day sequence, am - pm effect and corresponding interactions are not significant.

Digit Span Test:

The mean digit span responses are presented in Figure 13 and the analysis of variance in Table V. The digit span test has an additional forward - backwards variable which is labeled F B. Subjects in groups is a significant factor. Analysis of groups (not presented) shows that subjects was a significant source only in group 2. The backwards - forwards effect is highly significant with the forward mean response of 7.333 and the backward response of 6.000. Table V also calls attention to a significant day sequence effect. Figure 13 also illustrates this improvement in mean responses from day 1 to day 3 (averaging am and pm). TCE vapor concentration was not a significant source of variation and Figure 13 reveals mean responses of about equal magnitude for three TCE vapor concentrations. The forward - backward response pattern was not the same for all TCE vapor concentrations as shown in Table VI. The forward - backward differential decreases as TCE vapor concentration increases. All other sources of variation indicated in Table V are judged to be not significant.

Figure 12

Tachistoscopic Perception Mean Responses and 95% Confidence Intervals

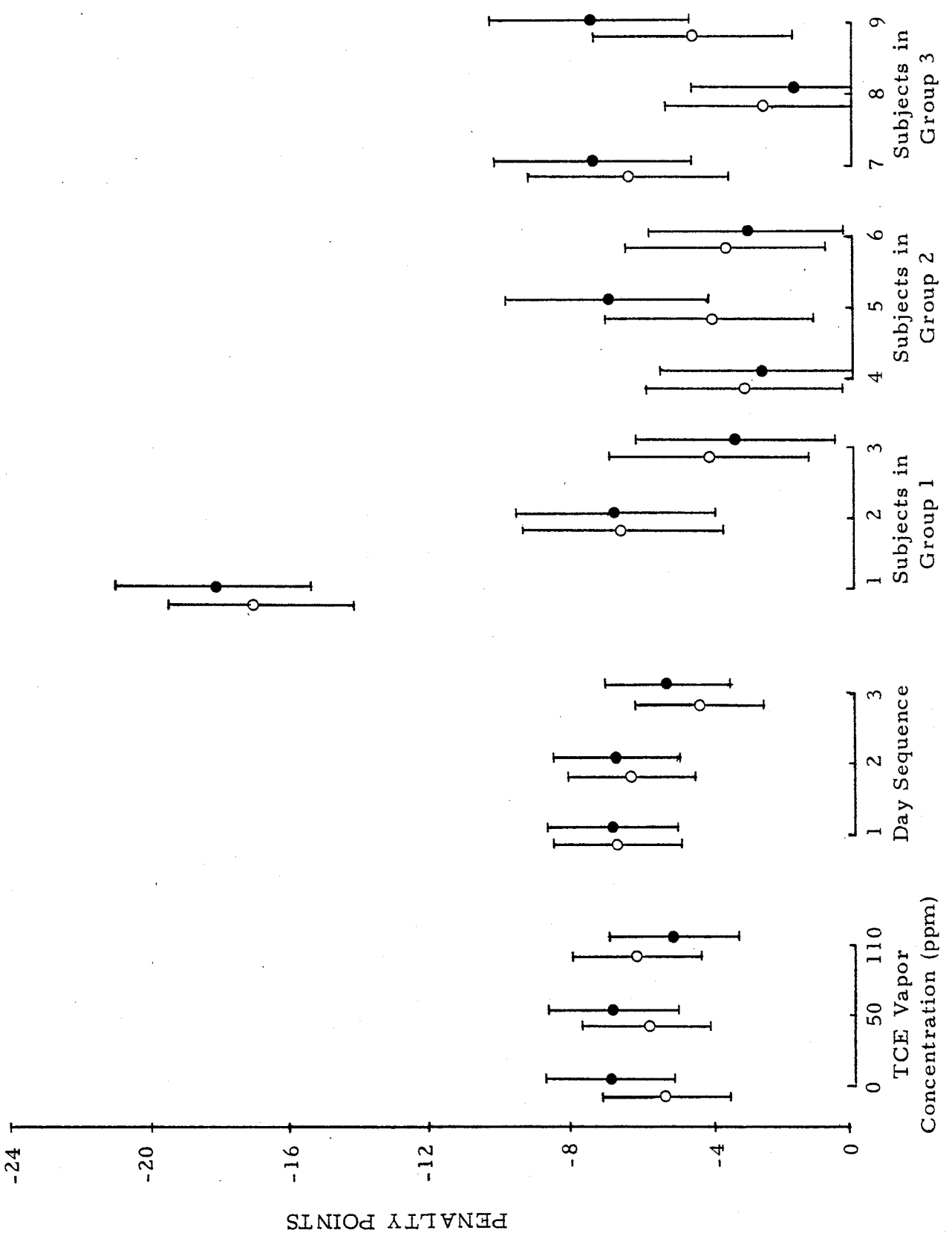

TABLE IV

FINAL ANALYSIS OF VARIANCE FOR TACHISTOSCOPE PERCEPTION

Source	DF	Sum of Squares	Mean Square	F Ratio	
Group	2	313.343	158.171	1.266	NS
Subjects in Groups	6	749.541	124.924	25.6155	P < .001
Day Sequence	2	38.620	19.310	3.214	NS
TCE	2	4.232	2.116	.352	NS
Residual Interaction	2	1.150	.575	.096	NS
Residual (1)	12	72.112	6.009		
am pm	1	3.375	3.375	.7112	NS
am pm x Group	2	1.861	.931	.1962	NS
am pm x Subjects on Groups	6	28.472	4.745	.9730	NS
am pm x TCE	2	18.361	9.180	1.8825	NS
am pm x Day Sequence	2	1.583	.791	.1623	NS
am pm x Residual Interaction	2	1.444	.722	.1481	NS
Residual (2)	12	58.523	4.876		

Figure 13

Digit Span Mean Responses and 95% Confidence Intervals

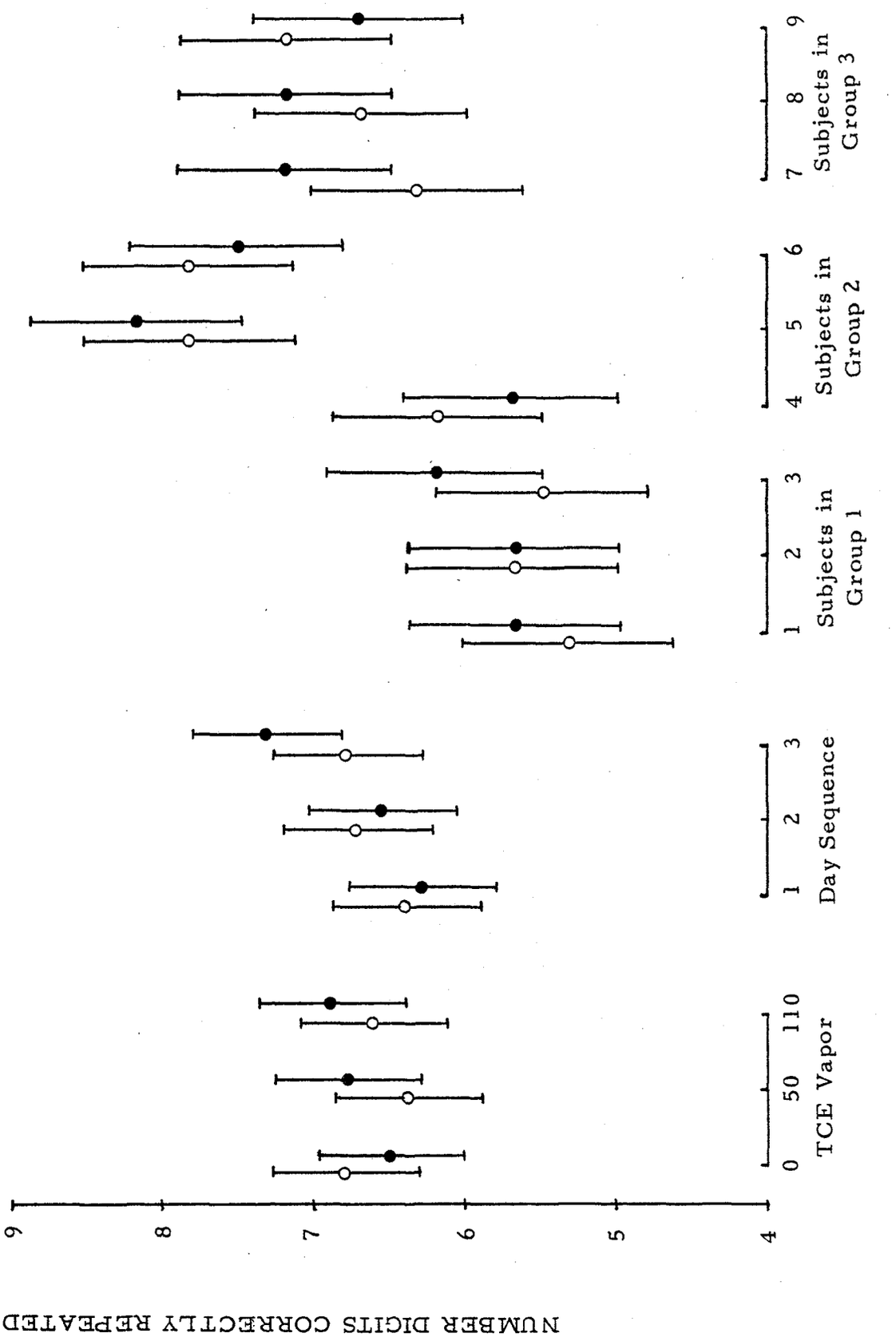

TABLE V

FINAL ANALYSIS OF VARIANCE FOR DIGIT SPAN TEST

	DF	Sum of Squares	Mean Square	F Ratio	
Groups	2	38.38852	19.1942	3.1745	NS
Subjects in Groups	6	36.27816	6.0463	10.1245	P < .001
Sessions in Groups	6	10.44484			
TCE	2	.72222	.3611	.4171	NS
DS	2	9.55555	4.7777	5.5190	P < .025
Residual Interactions	2	.16666	.0833	.0963	NS
Residual (1)	12	10.38852	.8657		
am pm	1	.33332	.3333	.5582	NS
am pm x Group	2	2.16707	1.0835	1.8144	NS
FB	1	47.99929	47.9992	80.37	P < .001
FB x Group	2	.50076	.2503	.4193	NS
A x FB	1	.92633	.9263	3.7053	NS
A x FB x G	2	1.24032	.6201	2.4806	NS
A x TCE	2	2.16667	1.0888	1.1361	NS
A x DS	2	2.16666	1.0888	1.1361	NS
A x Residual Interaction	2	3.66666	1.8333	1.9129	NS
FB x TCE	2	4.05566	2.0278	6.3488	P < .025
FB x DS	2	.22222	.1111	.3478	NS
FB x Residual Interactions	2	2.05566	1.0278	3.2149	NS
A x FB x TCE	2	.68488	.3424	.5733	NS
A x FB x DS	2	2.74033	1.3701	2.2942	NS
A x FB x Residual Inter.	2	.24166	.1208	.2023	NS
A x P in Groups	6	2.49964	.4166	.6976	NS
FB x P in Groups	6	6.83333	1.1389	1.9071	NS
A x FB x P in Groups	6	1.50002	.2500	.4186	NS
P x S x A in Groups	12	11.50040	.9584	1.6048	NS
P x S x FB in Groups	12	3.83339	.3194	.5348	NS
Residual (2)	12	7.16594	.5972		

TABLE VI

DIGIT SPAN MEAN RESPONSES

	TCE Vapor Concentration		
	0 ppm	50 ppm	110 ppm
Forward	7.555	7.222	7.222
Backward	5.722	5.944	6.333

Finger Dexterity:

The finger dexterity performance data are presented in Figure 14. Confidence intervals for subject means are large because the measure of variation used to determine interval length is differences between right and left hands. The analysis of variance for the finger dexterity (Table VII) reveals significance for subjects in groups, day sequence, and am - pm effect, but not for TCE vapor concentration or any other sources. Subjects differ significantly in groups 1 and 2 but not group 3 (analysis not presented). The effect of learning upon performance is illustrated by the improvement trend from day 1 to day 3 in Figure 14. The pm mean is consistently higher than the am mean, a significant am - pm effect confirmed in Table VII.

Flanagan Coordination Test:

The mean performance data are illustrated in Figure 15 and analysis of variance results are presented in Table VIII. The coordination test resulted in several significant sources of variation, namely: subjects in groups, day sequence, TCE vapor concentration, the am - pm x TCE interaction and am - pm x residual interactions. Table IV gives individual means for subjects in each of three sessions (days 1, 2 and 3). Subjects 5 and 6 have low test scores in session 1 (TCE, 110 ppm), which explains the significance of the interaction, day sequence and TCE vapor concentration factors. When interactions are significant the data should be separated into groups and attempts made to assess factors. However, TCE vapor concentration and

Figure 14

Finger Dexterity Mean Responses and 95% Confidence Intervals

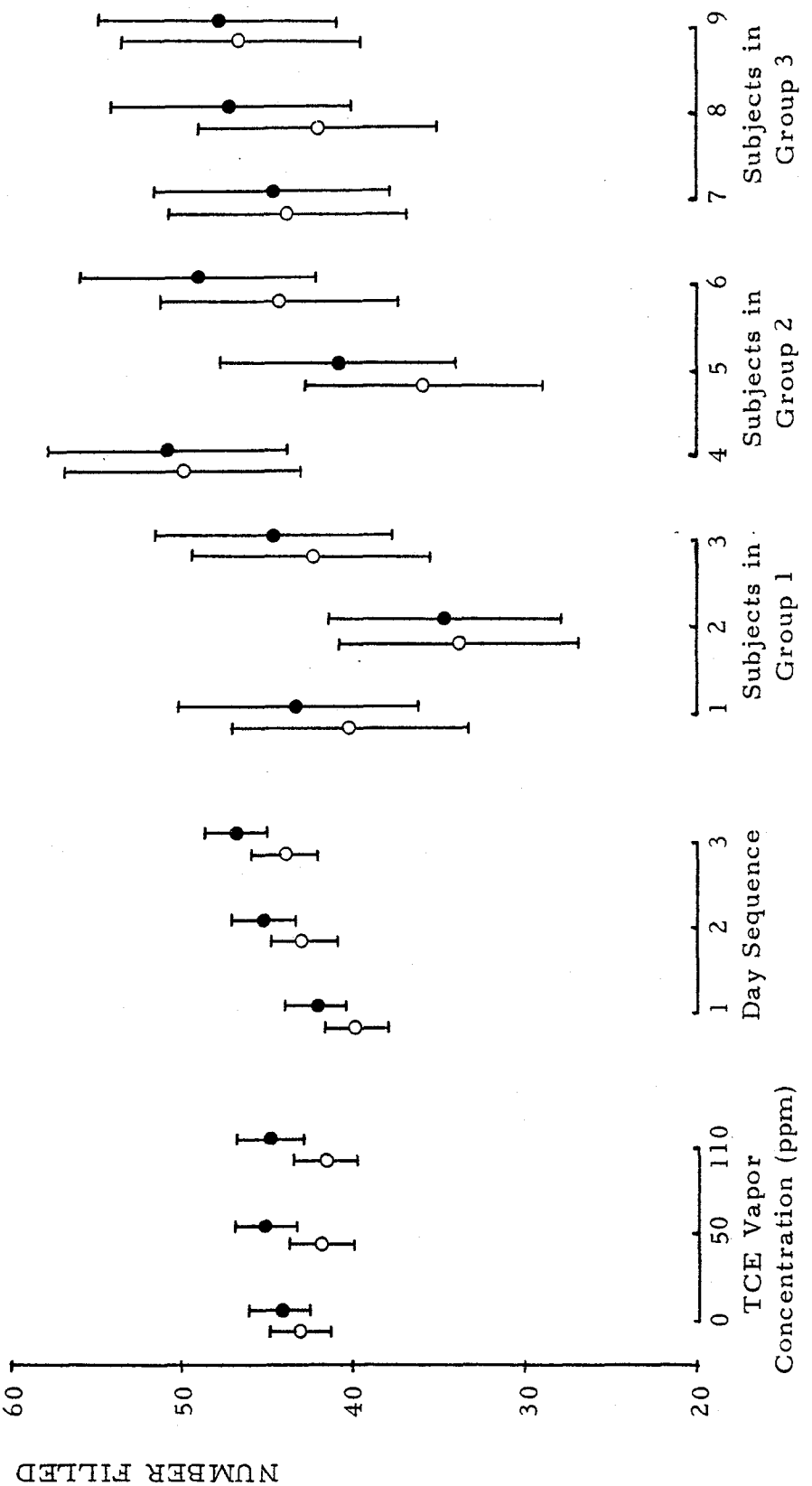

TABLE VII

FINAL ANALYSIS OF VARIANCE FOR FINGER DEXERITY

Source	DF	Sum of Squares	Mean Square	F Ratio	
Groups	2	723.185	361.092	2.8114	NS
Subject in Groups	6	1541.278	128.439	6.2261	P < .005
Day Sequence	2	372.074	186.037	16.9881	P < .001
TCE	2	4.463	2.232	.2038	NS
Residual Interaction	2	.074	.037	.0034	NS
Residual (1)	12	131.416	10.951		
am pm	1	171.259	171.259	21.3327	P < .005
am pm x Group	2	15.403	7.701	.9593	NS
Day Sequence x am pm	2	.963	.481	.0671	NS
TCE x am pm	2	10.907	10.453	1.4564	NS
Residual Interaction x am pm	2	5.629	2.814	.3921	NS
am pm x Subject in Group	6	48.167	8.028	.3892	NS
am pm x Subject x Session in Group	12	86.139	7.178	.3479	NS
Residual (2)	54	1114.000	20.629		

Figure 15

Coordination Test Mean Responses and 95% Confidence Intervals

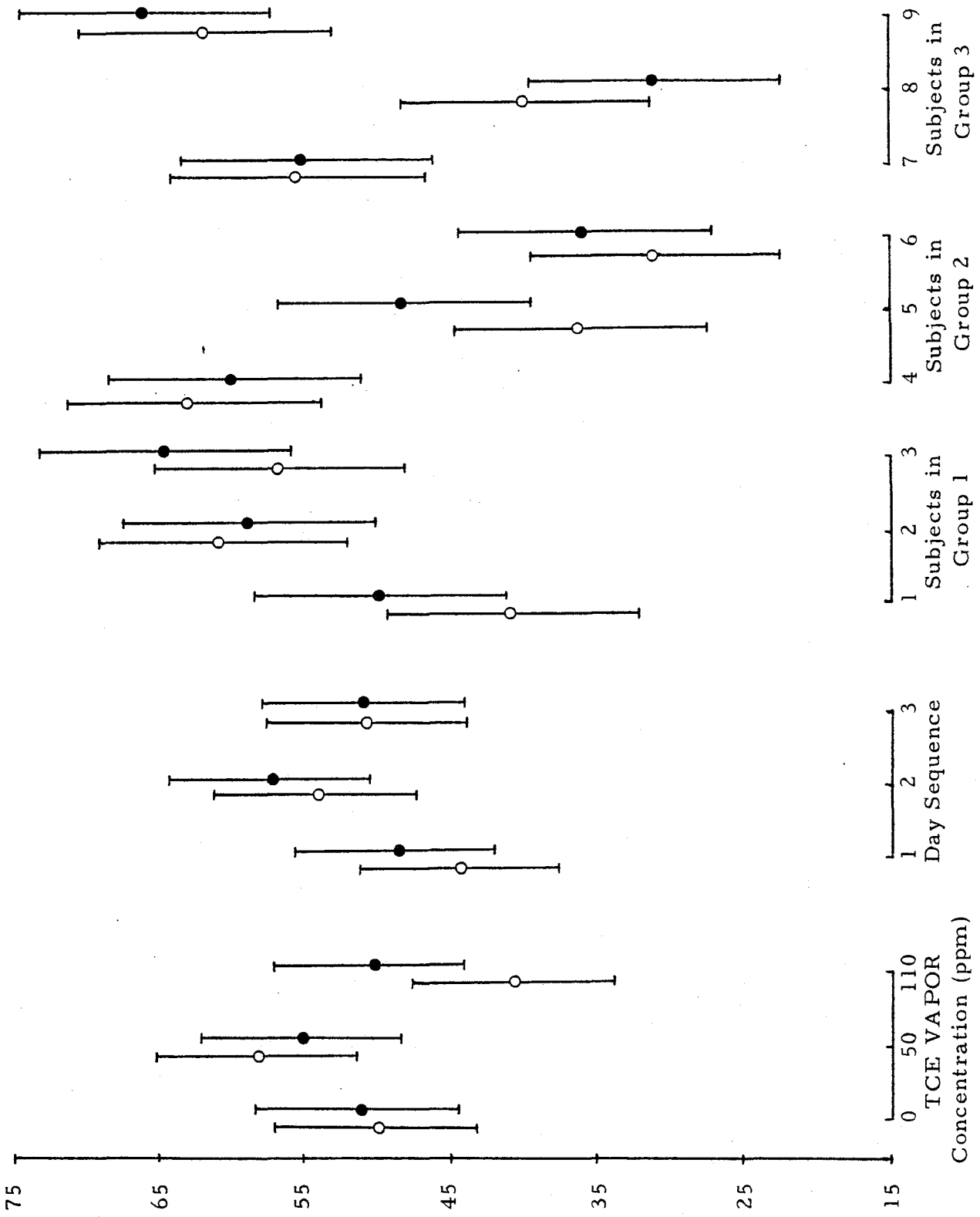

TABLE VIII

FINAL ANALYSIS OF VARIANCE FOR COORDINATION TEST

Source	DF	Sum of Squares	Mean Square	F Ratio	
Group	2	853.000	426.500	.4353	NS
Subjects in Group	6	5878.333	979.72	21.4	P < .001
Day Sequence	2	757.000	378.500	4.2382	P < .05
TCE Exposure	2	1159.000	579.500	6.4889	P < .025
Residual Interactions	2	277.325	138.663	1.5527	NS
Residual (1)	12	1071.666	89.306		
am pm	1	88.166	88.166	1.3105	NS
am pm x Group	2	120.333	60.166	.8943	NS
am pm x Subjects in Group	6	403.668	67.278	1.4670	NS
am pm x TCE	2	373.000	186.500	4.0666	P < .05
am pm x Day Sequence	2	39.000	19.500	.4252	NS
am pm x Residual Interaction	2	444.000	222.000	4.8407	P < .05
Residual (2)	12	550.332	45.861		

day sequence cannot be assessed in groups 1, 2 and 3 because of the aforementioned confounding. The low scores could be due to a genuine central nervous system depressant effect of the solvent in more sensative individuals or they could simply be low scores on the intial part of the learning curve. Statistically, TCE vapor concentration is a significant source. However, had TCE exorted a depressant effect, test scores would be expected to be lower or as low in the afternoon. Such was not the case. Differences between subjects is also obvious in Figure 15. Day sequence reveals a generally increasing score when days 2 and 3 are compared to day 1, all of which indicates that a test requiring multiple training sessions to reduce learning effect probably should not have been included in the test battery.

Digit Inspection Test:

Mean performance data for the digit inspection test are presented in Figure 16. Significant performance differences among subjects is evident and a learning trend is descernible. The analysis of variance (Table IX). reveals significant sources for subjects in groups, day sequence, residual interactions, the am - pm x TCE interaction and the day sequence interaction. The am - pm x TCE and am - pm x day sequence interactions are significant. Due to the overall experimental design, TCE vapor concentration and day sequence cannot be assessed for each of the groups, as they should be when interactions are significant.

Figure 16

Digit Inspection Test Mean Responses and 95% Confidence Intervals

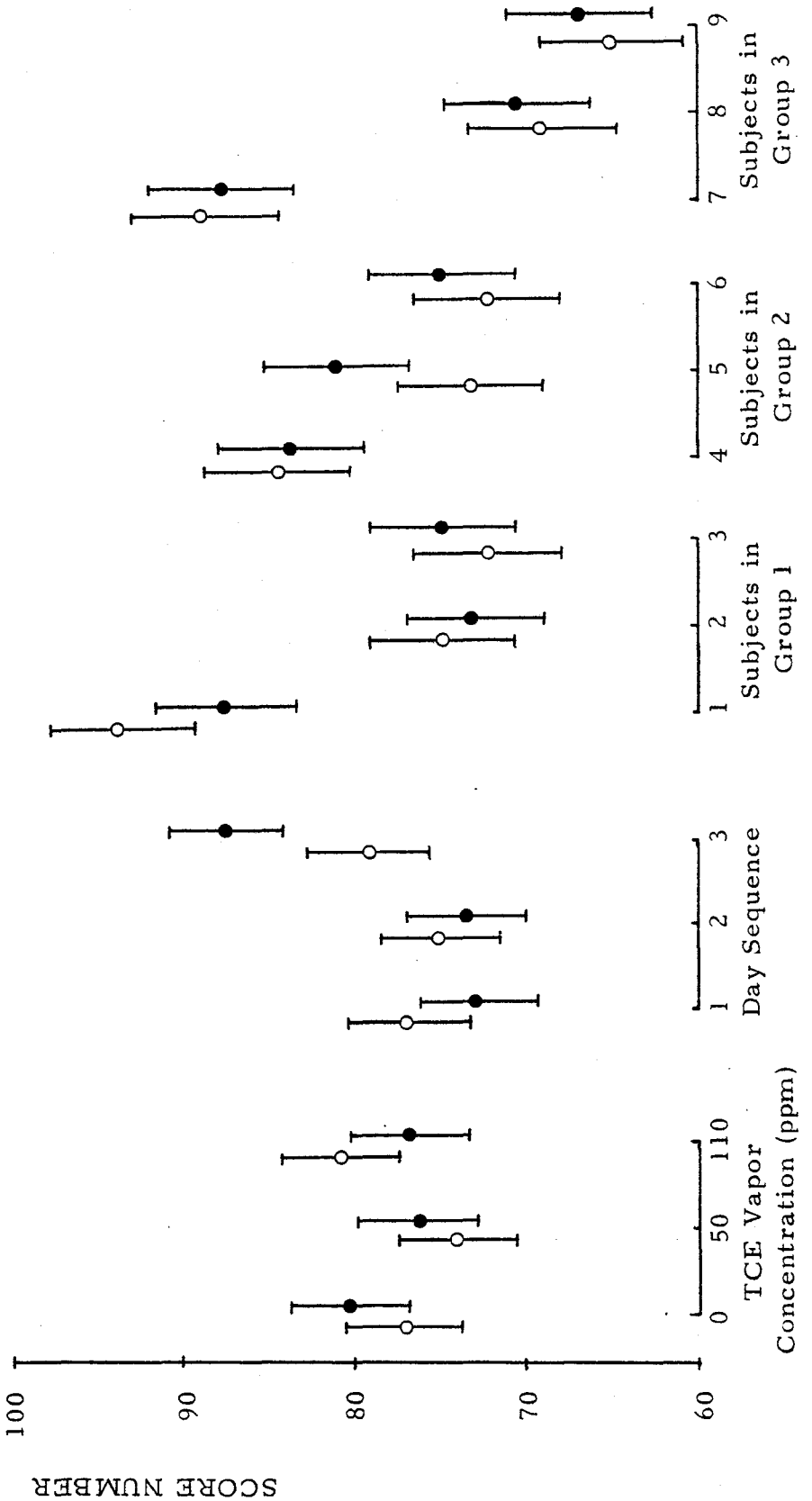

TABLE IX

FINAL ANALYSIS OF VARIANCE FOR INSPECTION TEST

Source	DF	Sum of Squares	Mean Square	F Ratio	
Group	2	231.4455	115.7225	.2145	NS
People in Groups	6	3237.2200	539.5367	45.7072	P < .001
Day Sequence	2	868.7777	434.3888	20.6761	P < .001
TCE Exposure	2	128.1111	64.0555	3.0489	NS
Residual Interactions	2	940.5571	470.2785	22.3846	P < .001
Residual (1)	12	252.1080	21.0090		
am pm	1	7.4074	7.4074	.3933	NS
am pm x Group	2	46.9259	23.4629	1.2458	NS
am pm x Subject in Group	6	113.0010	18.8335	1.5955	NS
am pm x TCE	2	102.9259	51.4630	4.3597	P < .05
am pm x Day Sequence	2	345.3704	172.6852	14.6291	P < .001
am pm x Residual Interactions	2	26.7037	13.3519	1.1311	NS
Residual (2)	12	141.6498	11.8042		

Summary of Behavioral Testing:

In each of the six behavioral tests administered variability among subjects was highly significant. This clearly suggests that experiments of this type must be designed to include more subjects and so minimize the effect of subject variation permitting more accurate assessment of the factors of interest (TCE). Four of the six tests produced evidence of learning as measured by day sequence (Digit Span, Finger Dexterity, Coordination and Digit Inspection). The am - pm differential (day fatigue) was significant for only one test (Finger Dexterity). TCE vapor concentration was an insignificant source of variation in five of six tests. TCE vapor concentration was statistically significant in the coordination test, a test which was also influenced by other interaction effects.

COMMENTS

This investigation failed to corroborate the Salvini, Binaschi, and Riva report that an acute 8-hour exposure to TCE 110 ppm resulted in a decrement in the performance of four behavioral tests. There are three technical reasons which could account for the differences in results between the two laboratories: questionable statistical analysis of the data, an inaccurate TCE vapor exposure, or poor experimental execution.

In the opinion of the authors, technical aspects of the analysis of variance tables in the Salvini, Binaschi and Riva paper (source of variation

breakdown and choice of some F-ratios) appear to be incorrectly performed. It is unfortunate that the Salvini paper fails to present mean test scores and other summary statistics because this lack of basic statistical information makes it impossible to either compare results (mean scores, magnitude and direction of observed differences) between papers or to make an independent assessment of the Salvini data.

There is some question about the adequacy of analytical control in the Salvini TCE vapor exposures. Intermittent atmoization of liquid TCE in a small chamber monitored intermittently with a gas sampling syringe through a small port in the entrance door sets the stage for an exposure which could feature wide unmeasured fluctuations in TCE vapor concentration. The failure to use a second independent analytical procedure with which to check the accuracy of the primary instrumentation coupled with the failure to monitor the TCE in the breath or blood of the subjects in the post-exposure period prevents a retrospective review of the accuracy with which the vapor exposures were performed.

The experimental design employed by Salvini and his co-investigators would have been stronger had it included exposure to two concentrations of TCE instead of a single one-time exposure to 110 ppm. At 110 ppm the chloroform-like odor of TCE vapor is strong and distinctive, precluding the performance of even a single-blind experiment. The use of a single concentration also precludes the establishment of a dose-response relationship. It is conceivable that highly suggestible individuals could be induced to perform

poorly once they were made aware of the CNS depressant effect of TCE.

Another troublesome feature of the experimental design of the Italian workers is the $1\frac{1}{2}$-hour lunch break during which time the subjects were free to leave the laboratory setting. Had the subjects imbibed wine, the blood stream concentrations of TCE would have been elevated dramatically[10-12]. Blood alcohol concentrations of 0.05%, concentrations easily achieved while drinking wine, could result in a doubling of the TCE blood stream concentration, converting the physiological effect of TCE 100 ppm to that of vapor concentration much higher.

In our study, the Flanagan coordination test and the random number inspection test were added to the Salvini battery of four tests for comparison purposes because they had been used in other TCE studies[11-12]. In retrospect the decision to do so was poor since the repetitive use of either test should be preceded by an adequate training period if the learning effect on performance is to be minimized. The experimental design of the Salvini experiment precluded this. Tow of the nine subjects who were exposed in their initial session to TCE 110 ppm had low coordination test scores. This could represent a definite CNS depressant effect of TCE or a low score on a normal learning curve or a biased subject response to exposure. This finding merits additional study, preferably in individuals who have been adequately trained so that the influence of learning on test scores can be eliminated as a variable.

It was of extreme interest to observe the wide variation in subjective

responses reported by the subjects (Table II). Note that two reported headache and lightheadedness the first time they were placed in the controlled-environment chamber, though they were not exposed to TCE. This re-emphasized the role of suggestion in creating subject bias and the danger of studying a single TCE concentration.

Salvini and his co-investigators were critical of the human response data of Stopps and McLaughlin because they had failed to simulate an 8-hour working day when exposing subjects to TCE for fewer than 8 hours[14]. Continuing with the same reasoning, Salvini, et al, may be admonished for drawing conclusions regarding TCE effect without having simulated a work week which is essential when evaluating the effect of a solvent which builds up in body tissues with repeated, daily 8-hour exposures[4,11]. Therefore, the judgment regarding the adequacy of the present TLV to protect workmen from TCE-induced behavioral performance decrement must be held in abeyance until data from individuals repeatedly exposed are available.

FIGURE CAPTIONS

Figure 1: Panel of the Complex Reaction Time Test.

Figure 2: Subject performing the Complex Reaction Time Test.

Figure 3: Investigator recording the reaction time for the 42 stimuli comprising the Complex Reaction Time Test. The subject performing the test can be seen in the controlled-environment chamber on the other side of the observation window.

Figure 4: Subject performing the Tachistoscopic Perception Test.

Figure 5: Subject seated in the audiometric booth performing the Digit Span Test.

Figure 6: Carrel within the controlled-environment chamber where the Finger Dexterity Test was performed.

Figure 7: Subject performing the Finger Dexterity Test.

Figure 8: Flanagan Coordination Test.

Figure 9: Digit Inspection Test.

Figure 10: The concentration of trichloroethylene in the expired breath was monitored following each vapor exposure. Note the separation between the two exposure concentrations. These data are in close agreement with those previously published [11, 12]. These breath data confirm that vapor exposure to 50 ppm and 110 ppm did occur.

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