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13. ABSTRACT

This paper was presented at the Proceedings of the 1st Annual Conference on Environmental Toxicology, sponsored by the SysteMed Corporation and held in Fairborn Ohio on 9, 10, and 11 September 1970. Major technical areas discussed included toxicological evaluation of carbon monoxide, methodology, pathology, atmospheric contaminants, and toxicology of propellants and other military chemicals.

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PAPER NO. 3

HUMAN SLEEP PATTERNS AND PSYCHOMOTOR PERFORMANCE DURING EXPOSURE TO MODERATE CONCENTRATIONS OF CARBON MONOXIDE

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INTRODUCTION

Carbon monoxide (CO) effects are generally believed to be mediated through tissue hypoxia (Dinman, 1968). Since the central nervous system is extremely sensitive to oxygen deprivation, it would be expected that even low level exposures to CO would produce observable changes in human performance. Yet experimentation in this area has not produced as clear a picture as one would have expected.

It is accepted that subjective symptoms of CO exposure rarely occur below carboxyhemoglobin (COHb) levels of 20 percent, while most acute signs of cardiovascular, respiratory, and central nervous system embarrassment occur at COHb levels greater than 30 percent (Haldane, 1927). However, a number of investigators have indicated that human performance is impaired at COHb levels as low as 2 to 5 percent. Visual discrimination was measured by MacFarland, Roughton, Halperin, and Niven (1944) who demonstrated impairment with COHb levels of 4 percent. Similarly, Lilienthal and Fugitt (1946) reported impaired flicker fusion at 6,000 feet with COHb levels of 5 to 10 percent. However, another study (Vollmer, King, Birren and Fisher, 1946) found no changes in flicker fusion, visual perimetry, or ataxia as a function of COHb level up to 22 percent at simulated altitudes of 10 and 15 thousand feet.

With respect to cognitive and psychomotor performance, impairments in mental arithmetic and other functions have been found by Schulte (1963) at 5 percent COHb, with some tendency for disruption as low as 2 percent. Beard and his co-workers have shown decreased auditory discrimination of tone length with COHb levels of approxi-

18

mately 4 to 5 percent (Beard and Wertheim, 1967). On the other hand, Dorcus and Weigand (1929) found no decrements in cognitive functioning or psychomotor tasks with COHb levels as high as 25 to 35 percent. A recent study similarly found no decrement in psychomotor performance, and no disruption of the subjective time estimate of a ten-second interval with COHb level as high as 7 percent (O'Donnell, Mikulka, Heinig, and Theodore, 1970). Stewart et al (1970) found no significant performance effects in males exposed to 100 ppm CO for 9 hours. Obviously, additional work is needed to clarify the reasons behind these apparently contradictory results.

The present study represents an attempt to address this question from both a traditional and novel viewpoint. In addition to a battery of psychomotor tasks, all of which have been used in previous research on CO, a different approach to CO research in performance was introduced on a pilot basis. The subject's sleep patterns were monitored continuously during an all-night exposure to CO, and data were analyzed to determine whether the exposure had any effect on these sleep patterns. Sleep patterns have been shown to be extremely sensitive to central nervous system conditions, and to change markedly with small variations from the normal (Foulkes, Metcalf, and Stoyva, 1968; Foulkes and Hobson, 1969). The existence of normal sleep patterns is dependent on several important structures of the brain, including the reticular formation, limbic system, hypothalamus, thalamus, and, importantly, the cerebral cortex (Zanchetti, 1967; Zung, 1970; Roffwarg, Muzio and Dement, 1966). Biochemically, it appears that the various phases of the sleep-wakefulness cycle depend on the relative concentrations of serotonin and norephinephrine, and/or related substances (Torda, 1969). In view of these facts, it would seem that if CO has any effects on the central nervous system which would be severe enough to show up as performance decrements, then these effects should certainly manifest themselves in alterations of the subjects' sleep patterns. Since this approach had never been tried before, and since the monitoring of sleep patterns is a complex and experimentally time consuming procedure, it was decided that a pilot study would be done using the smallest number of subjects usually necessary to uncover practically important effects on sleep patterns.

PROCEDURE

Subjects

Four volunteer male subjects were used in the present study. All subjects were members of the U.S. Air Force, all had undergone altitude training, and all had a currently validated class III flight physical. Subjects' ages were 20, 24, 24 and 42. All of the subjects were known to be non-smokers, and baseline carboxyhemoglobin (COHb) determinations supported this observation.

Environment

All CO and control exposures were carried out in the Thomas Domes of the Toxic Hazards Division, Wright-Patterson Air Force Base, Ohio. Each dome is a completely closed environmental system into which a given contaminant can be introduced and maintained within ± 3 percent of desired concentration. Air flow during the present study was controlled at 20 ft^3/min. The dome is circular with a diameter of 12 feet and a total volume of 828 ft^3. CO level was continuously monitored by a non-dispersive infrared analyzer. Temperature was maintained between 68 and 74 F, and in order to maintain a perfect seal on the dome, a slight negative pressure (680 mm Hg) was held throughout all exposures. Subjects entered the dome through an airlock which allowed the interior environment to remain stable.

Performance Measures

Critical flicker fusion (CFF) was measured by having the subject binocularly and centrally view a red test light 0.375 inch in diameter from a distance of approximately 16 inches. Using the method of limits, the subject adjusted the flicker rate of the light until it just appeared to be a steady light. The actual flicker rate was measured by a Monsanto Model A-100 digital frequency counter. A total of 12 CFF readings were obtained in this way each day for each subject.

The subject's ability at mental arithmetic was measured by using the "solar radiation" test from the School of Aerospace Medicine Neptune Battery. This test, and all subsequent Neptune tests are explained in detail by McKenzie, White and Hartman (1969). Basically, the subject is required to add four one-digit numbers, to add the two digits of that answer. Scoring is in terms of the time necessary to correctly solve a problem, as well as the errors for each problem. In the present study, a total of 20 problems were given to the subject each day.

In order to test the subject's ability to perform tasks under varying workload conditions, two other tasks from the Neptune Battery were used. In one set of tests, referred to as "moderate" workload tests, the subject was required to track a needle dial and to keep it centered within small limits. A sine-wave forcing function was fed into the dial, producing essentially a first-order tracking task. While performing this task, the subject was also required to monitor three other dials located above the tracking dial. At eight randomly selected times during the tracking trial, one of these dials would go off-center. The subject was required to press the correct one of six buttons to return the dial to center. One trial on this moderate workload test lasted one minute, and two trials were obtained each day. The tracking task was scored in terms of total time off target. For the monitoring task, scoring was in terms of the total time taken to see and respond to the offset dials.

Another group of tasks was referred to as the "high workload" test. The same two tasks from the Neptune battery were used, but in addition, the subject was required to simultaneously perform another task. Essentially, he had to monitor three lights which flashed in random order. His task was to note and remember how many times each of the lights flashed during the one-minute tracking trial. At the end of the trial, he was required to indicate his answer for each light. This test was used solely to add an additional workload on the subject, and was not scored. However, subjects were not informed of this fact, and were instructed to give equal attention to all the tasks in each test.

Because some past studies have indicated that one of the effects of CO exposure is a marked change in the individual's subjective time estimate, three tests were included to measure the subject's ability to estimate time in various ways. In the first of these, the procedure used in a previous study (O'Donnell, Mikulka, Heinig and Theodore, 1970) to determine the subjective estimate of "empty" ten-second time interval was used. In this test, the subject pressed a button each time he estimated that ten seconds had elapsed. These estimates were carried out for two three-minute periods each day. In the second test of this series, the subject was required to hold the button down for an estimated 30 second interval, then release it. He then began another 30 second estimate at will. Four such estimates were obtained twice each day for each subject. The last time estimation task required the subject to compare the length of two tones presented in rapid sequence. The tones were 1, 000 cycle pure tones presented to both ears at 85 ± 2 db. The first, or standard tone, was always 1.00 seconds in length, and the second tone varied between 0.675 and 1.325 seconds in 0.025 second intervals. The interval between tones was 0.5 second. For each test, 27 determinations were made by the method of constant stimuli, with 9 comparison tones longer, 9 shorter, and 9 equal to the standard tone. Two such tests were given to each subject each day.

Sleep Measures

The procedures recommended in the standardized manual for recording and staging sleep (Rechtschaffen and Kales, 1968) were followed in the present study. Beckman bio-potential electrodes were attached to the shaved scalp at the C_3 and C_4 positions for electroencephalographic (EEG) recording. Both of these electrodes were referred to the left mastoid. Grass silver cup electrodes were placed at the outer canthus of each eye and referred to the left mastoid to obtain two channels of electro-occulographic (EOG) records. Two Grass silver cup electrodes were placed on the muscle areas on and beneath the chin (mental-submental) to obtain a single channel of electromyographic (EMG) records. Finally, for medical monitoring purposes, two electrodes were placed on the chest to obtain a single channel of electrocardiogram. Wires from all electrodes were bundled at the top of the subject's head and plugged into an electrode board near the bed. No subject reported unusual discomfort with this electrode placement, and except for two instances where electrodes came loose during the night, recording of the physiological measures was uneventful.

Signals were recorded on a Grass Model 78 recorder. Records were printed out continuously at 15 mm/sec. Scoring was done independently by two trained scorers using the criteria set forth in the standardized manual (Rechtschaffen and Kales, 1968). Agreement between the scorers on a page by page basis, including all stages separately, was between 90 and 95 percent. For the sleep data presented here, the scoring of the author was used.

Design and Testing Procedures

Each subject slept for 9 nights in the Thomas Dome. The first four nights were used to adapt the subject to the environment and to insure that all baselines were stable. This procedure was necessary since there is a strong "laboratory" effect on sleep patterns which, under normal circumstances, takes several nights to stabilize. In the relatively high noise environment of the dome, in a situation where the subject might have some apprehension, it was necessary to use four complete nights for such adaptation. Beginning on the fifth night, a double-blind procedure was instituted. Neither the subjects, nor experimenters, nor technicians working in the area knew whether CO was present on any given night. Only the chemist-monitor, located remotely from the dome, was aware of the environmental status.

For the five experimental nights, two exposure nights at either 75 or 150 ppm of CO were given. After each exposure night, a "blank" night with no CO present was given. This was done to insure that there would be no residual effect on the dependent variables from the CO exposure. Finally, a control night at 0 PPM of CO was given. Thus, no CO night was followed by another CO night, nor was a CO night followed by the control night.

Subjects entered the dome at 11 o'clock each evening. Electrode placement and final calibration took about 10 minutes, and the lights in the dome were usually turned out by 11:15. Sleep monitoring was begun from that point and continued, uninterrupted, until the subject was awakened at 6 A. M.

After waking the subject, approximately 30 minutes were spent in removing electrode wires, eating, etc., while the contaminant level was maintained. The subject then began the series of performance tests which were all located in the dome.

The first test given was the CFF test. This was followed by mental arithmetic, comparison of tone lengths, the moderate workload Neptune test, 10 second time estimate, the high workload Neptune test, and 30 second time estimate. The subject was then given a 5-minute rest, and the entire series of tests was repeated in reverse order. Total testing time was approximately 1 1/2 hours, so that the series ended at approximately 8 A.M. At this point, 10 ml of blood was taken for COHb, hematocrit and hemoglobin determination. The subject was then removed from the dome, taken to an adjoining room, and required to breathe 100 percent oxygen for one hour.

RESULTS

Carbon Monoxide Exposure Levels

Carboxyhemoglobin (COHb) determinations were made on the venous blood for each subject after each experimental session. These determinations were done by a modified gas chromatographic method of Dominguez, Christensen, Goldbaum and Stembridge (1959). The results of the COHb analyses are presented in table I. From this table, it can be seen that the COHb levels reached after approximately nine hours of exposure reflect a direct relationship with the level of ambient CO. It should be pointed out, however, that these values are somewhat lower than those which would be predicted from the use of theoretical curves generally available. However, these curves usually assume a relatively high ventilation and pulse rate, whereas during sleep these values are usually quite low. This would account for the unexpectedly low COHb levels found here.

TABLE I

FINAL CARBOXYHEMOGLOBIN LEVEL (PERCENT) AT EACH EXPOSURE LEVEL

SUBJECT	0 PPM	75 PPM	150 PPM
1	0.5	6.8	11.9
2	0.5	5.1	12.9
3	0.7	6.4	14.3
4	0.8	5.2	11.6
MEAN	0.6	5.9	12.7

Performance Measures

Time Estimation: In order to test the hypothesis that low level exposure to CO affects the estimate of subjective time, three different tests were administered. In the first test, the subject was required to estimate the passage of 10 second intervals by pressing a button, releasing it, and waiting the estimated amount of time before repeating the procedure. In the second test, the subject was required to hold the button down to estimate four 30-second intervals. In the third test, the subject was required to determine whether the second of two 1,000 cycle tones was longer or shorter than the first or standard tone.

Data on these three tests are presented in table II. With respect to the 10-second estimates, it can be seen that the interval was overestimated under all conditions. None of the differences was significant, and the only possible trend appeared to indicate that estimates were becoming more "accurate" under the CO conditions. Inspection of the data from individual subjects revealed that in 3 out of the 4 cases under each CO condition, the estimates were closer to the 10-second "real" time than under the control condition. For the 30-second estimates, it is again seen that no significant differences appeared between the control and CO groups. Further, no consistent trend appeared other than overestimation under all conditions. Individual subject's estimates appeared to follow no pattern related to the presence or absence of CO.

TABLE II

TIME ESTIMATION AFTER EXPOSURE TO CO CONDITIONS

TEST		0 PPM	75 PPM	150 PPM
10 Second Estimate (Seconds)	MEAN SD	11.43 1.72	10.58 1.51	10.38 1.25
30 Second Estimate (Seconds)	MEAN SD	35.59 5.32	35.82 5.25	34.51 5.97
Comparison of Tone Lengths (Errors)	MEAN SD	6.37 4.22	6.13 2.30	6.50 1.54

The tone comparisons were scored simply as correct or incorrect responses. As can be seen from table II, the mean differences between groups in the number of errors were small and did not reach statistical significance in any case. There were slightly fewer errors under 75 ppm CO than under the control condition, and slightly more errors under 150 ppm than under the control condition. Individual subjects' estimates revealed an almost random pattern with respect to CO condition, with 5 of the 8 CO exposures producing fewer errors than their respective controls. In summary, then, it can be seen that the present study cannot support the hypothesis that CO at these exposures produced a decrement in time estimation. Further, from the present data, there is no reason to suspect a trend to such an effect.

Critical Flicker Fusion (CFF): In addition to the above tests, a test of CFF was given to the subject. Each subject made 12 determinations of the CFF point each day and the mean of these determinations was calculated as his CFF point. These individual means were then combined to form the group means which are presented in table III. Again, it can be seen that none of the differences were significant, and that no consistent trend toward lower CFF values was seen as a function of CO exposure. Looking at individual subjects' data, no trends were apparent. In two of the four cases under each CO condition, subjects had higher (better) CFF scores than under the control condition. It therefore must be concluded that the present study failed to find any effect of CO on critical flicker fusion.

TABLE III

CRITICAL FLICKER FUSION AFTER EXPOSURE TO CO CONDITIONS

TEST		0 PPM	75 PPM	150 PPM
CFF (Cycles Per Second)	MEAN	40.60	40.30	40.80
	SD	5.78	4.73	6.16

Cognitive and Psychomotor Tests: The final series of performance tests administered to each subject was designed to probe a complex of cognitive and psychomotor functions. In the first of these tests, the subject was required to perform 20 arithmetic calculations, each involving additions and multiplications, and calling for use of short term memory. In addition to this test, two tests involving identical tasks but under different workloads were presented to the subject. In one case, he was required to track a needle dial to keep it centered, while a sine wave forcing function offset the dial. At the same time, he was required to monitor three dials and to correct any dial which went off center by pressing one of six switches. The scores for these two tests were the total time off target for the tracking task, and the cumulative time to respond to the dials in the monitoring or vigilance task. In the second test of this series, the subject was required to perform the same two tasks as above. At the same time, he was required to watch three lights and keep track of the number of times each light flashed during the trial. This task was not scored, since it was included simply to add an additional workload on the subject. Subjects had been instructed to give equal attention to all the tasks.

The results of these three tests are presented in table IV. Looking first at the mental arithmetic task, it can be seen that the total mean time to solution was slightly less under 75 ppm and slightly more under 150 ppm than under the control condition. In neither case were the differences significant. For the individual subjects, 7 of the 8 CO exposures produced better mental arithmetic scores than their respective controls. It therefore seems clear that for this extremely complex mental arithmetic task, exposure to CO for these durations had no detrimental effect.

TABLE IV

COGNITIVE FUNCTION AFTER EXPOSURE TO CO CONDITIONS

TEST		0 PPM	75 PPM	150 PPM
MENTAL ARITHMETIC (Time to Solution in Seconds)	MEAN	92.38	89.78	98.60
	SD	15.73	15.82	17.33
MODERATE WORKLOAD				
Tracking (Time off target, sec.)	MEAN	20.40	17.26	23.17
	SD	6.29	6.41	8.15
Vigilance (Cum. time to action, sec.)	MEAN	22.90	27.60	23.15
	SD	2.55	9.48	3.34
HIGH WORKLOAD				
Tracking (Time off target, sec.)	MEAN	27.73	22.40	25.00
	SD	5.64	5.09	5.19
Vigilance (Cum. time to action, sec.)	MEAN	37.30	42.90	31.40
	SD	9.63	14.33	11.55

Considering now the tasks listed under "moderate workload" it can be seen that again none of the comparisons for either task was statistically significant. For the tracking task, performance was slightly better under 75 ppm CO, and slightly worse under 150 ppm CO than under the control condition. The vigilance scores similarly showed no significant differences as a result of CO exposure. Under both CO conditions the mean scores were slightly worse than under the control condition; however, inspection of the scores for individual subjects revealed that in 5 of the 8 cases, performance was better under CO than in the control condition.

In the tasks listed under "high workload", tracking was slightly better under both CO conditions. Vigilance was worse under 75 ppm exposure and better under 150 ppm. Again, none of these differences was statistically significant.

It is interesting to note the effect of the additional task in the "high workload" tests. It can be seen by comparing identical tasks under both conditions that, as would be expected, the high workload condition produced uniformly worse scores. For the vigilance task, this effect was particularly noticeable, resulting in a mean total of 12.65 additional seconds to respond during the high workload condition. The difference in vigilance score between the two workload conditions was significant at the .05 level. This indicates that the addition of one task to a battery of two tasks as used here resulted in a greater effect on performance than all of the CO used in the present study.

Sleep Measures

The primary analyses planned for the sleep data in the present study were designed to answer the question of whether there was a change in the overall sleep pattern of subjects under carbon monoxide. These data will be presented here, while more intensive analyses of specific questions relating to the subjects' sleep will be presented at a later date. Figure 1 presents the mean percentage of total sleep time spent in each of the stages of sleep, along with the ±1 SD bar. Obviously, none of the differences between the control group and either CO group, or between the two CO groups, are significant. Inspection of the figure reveals that the differences between groups which do appear are so small, even in absolute terms, as to be negligible.

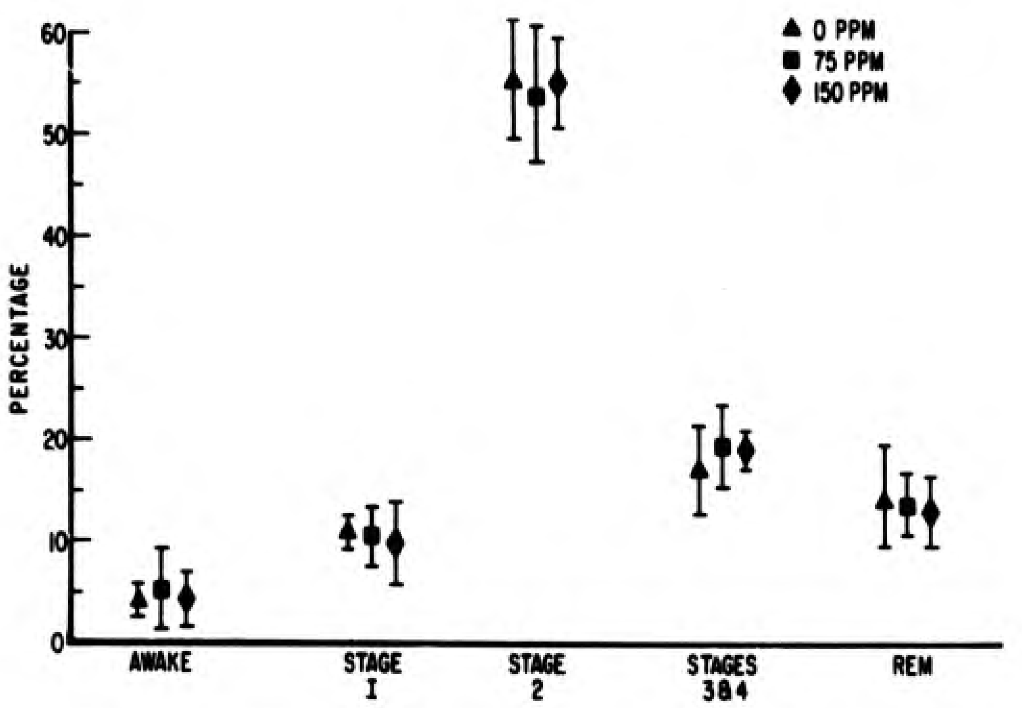

Figure 1. PERCENTAGE (± 1SD) OF TOTAL SLEEP IN EACH STAGE (WHOLE NIGHT).

In order to further determine whether there was a change in the overall sleep pattern due to CO exposure, the last three hours of the night were looked at separately. By this time, the subjects' COHb levels had reached a high point, and presumably any effects which would show up would be most evident. The data for these time periods are presented in figure 2. Although none of the comparisons was significant, there does appear to be some separation between the CO and control groups in stages 1 and 2. The data for individual subjects revealed no consistent pattern for stage 2 sleep, but subjects in all eight CO exposures showed less stage 1 sleep than they had in the control condition.

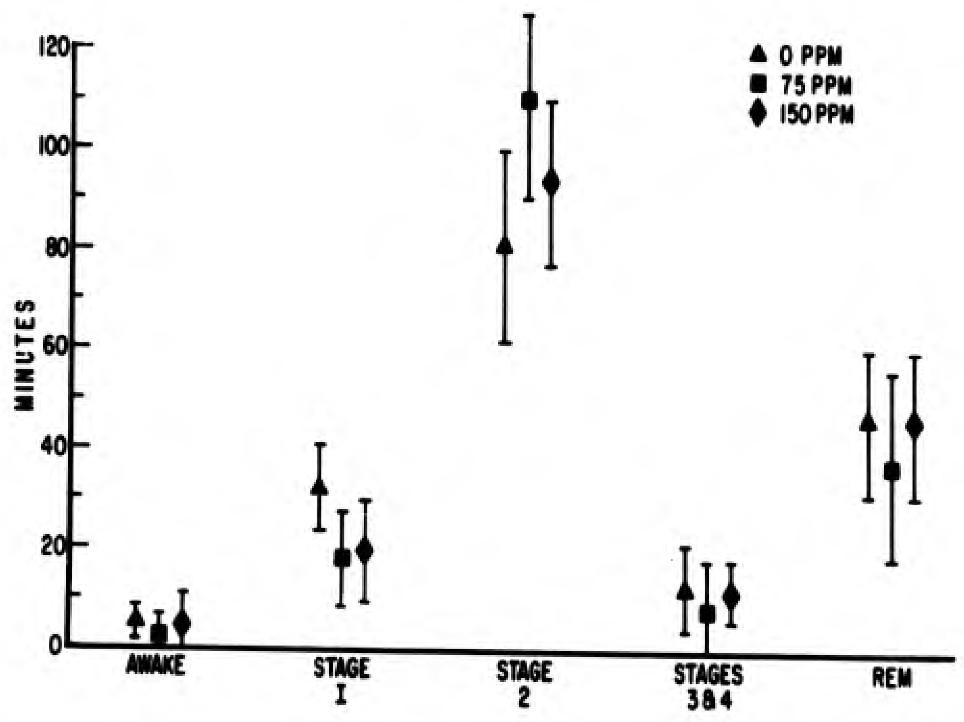

Figure 2. MINUTES (± 1SD) SPENT IN EACH STAGE OF SLEEP DURING LAST THREE HOURS OF CO EXPOSURE.

It is possible that CO exposure could have affected sleep in ways which would not be evident from an analysis of the total pattern. For this reason, several other analyses were done on the sleep data. In the first of these analyses, the mean number of times subjects entered the various stages during the course of the night were compared under differing CO conditions. These data are presented in table V. Again, none of the comparisons was significantly different between exposure conditions. It was noted, however, that in every stage of sleep, there were fewer stage changes in both CO conditions than there were in the control condition. This would provide an extremely tentative indication that there may have been slightly less "mobility" or restlessness under CO than in the control condition.

TABLE V

MEAN NUMBER OF TIMES IN EACH SLEEP STATE
DURING CO EXPOSURE CONDITIONS

STAGE		0 PPM	75 PPM	150 PPM
Awake	MEAN	6.00	4.75	4.50
	SD	2.35	2.28	3.20
1	MEAN	19.00	17.50	14.75
	SD	4.64	7.63	6.14
2	MEAN	18.25	17.00	17.00
	SD	2.49	4.06	2.55
3&4	MEAN	10.50	10.25	9.00
	SD	1.66	4.09	1.87
REM	MEAN	9.75	8.50	9.00
	SD	5.40	4.33	4.74

In order to probe this possible effect further, the mean duration of each stage of sleep during the night was determined. Thus, the total amount of time spent in each stage was divided by the number of times the subject entered that stage. These data are presented in table VI. None of the comparisons was significantly different from each other. There was a trend toward longer times spent awake and in stages 1, 2, and 3, under the CO conditions, and slightly shorter times spent in stages 4 and REM under CO. This result would indicate that if the previous indication of less mobility under CO is correct, than this is achieved by spending longer periods of time in the lighter stages of sleep. Obviously, lacking statistical significance, no definitive statements can be made. However, the above observations warrant further study.

TABLE VI

MEAN DURATION OF SLEEP STATES (IN MINUTES) DURING CO EXPOSURE CONDITIONS

STAGE		0 PPM	75 PPM	150 PPM
Awake	MEAN	2.70	3.75	4.85
	SD	.66	1.80	4.25
1	MEAN	2.30	2.43	2.58
	SD	.44	.48	.19
2	MEAN	11.60	12.85	12.68
	SD	1.16	3.64	2.03
3	MEAN	5.30	7.00	7.10
	SD	1.50	4.10	3.04
4	MEAN	12.00	10.90	11.00
	SD	10.00	4.42	3.06
REM	MEAN	9.35	8.75	7.68
	SD	5.86	3.35	2.60

CONCLUSIONS

It would appear that when subjects are allowed to sleep for a normal period of time in the presence of CO at a level up to 150 ppm, there is no major disruption of either their sleep patterns or subsequent psychomotor performance involving time estimation, mental arithmetic, tracking, or vigilance under either moderate or high workloads. With respect to the performance measures, no patterns were isolated which would indicate that more detailed study under the same conditions would yield any significant effects of CO exposure. Some extremely tenuous indications of possible changes in the mobility of subjects during their early stages of sleep were uncovered, and these should be investigated further.

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DISCUSSION

MR WANDS (National Academy of Sciences): What was the average duration of time after entry until the carboxyhemoglobin level was determined? They entered at 11 o'clock, I believe you said, but I did not catch the exit time.

CAPTAIN O'DONNELL (Aerospace Medical Research Laboratory): It was approximately 8 o'clock in the morning, so it would be approximately nine hours exposure. The level was taken at the end of exposure.

DR. BEARD (Stanford University Medical Center): What was the noise level in the domes?

CAPTAIN O'DONNELL: The noise level was fairly high, I think it's around 84 db, 85 db. Out of the cone it would be less.

DR. MAC EWEN (SysteMed Corporation): Our dome tops act as parabolic reflectors of noise. The noise in the center of the dome is 85 db and in some sections is perhaps even higher. At the periphery, where the man in the bed was, the noise level was probably 60 to 65 db based on previous measurements made under these conditions.

CAPTAIN O'DONNELL: I might mention that at first we asked the subjects very thoroughly whether the noise seemed to bother their sleep and, subjectively, none of the subjects reported that the noise bothered their sleep beyond the first night. This was one of the reasons why we gave four nights of adaptation to the dome. Sleep obviously is very sensitive to changes in location and we wanted to give enough nights so that the subject would be completely stabilized and, in fact, that happened within about three nights.

DR. AZAR (E. I. duPont de Nemours and Company): I was wondering if you looked into any effect of learning on your psychomotor tests because it appeared that on several instances that under carbon monoxide the scores tended to improve, and if your subjects were learning the psychomotor tests and then you compared test scores with their control levels, if there was a subtle effect of carbon monoxide you wouldn't have picked this up unless you looked at a learning trend.

CAPTAIN O'DONNELL: There would be two things on that. The first thing is that we tested the subjects on the tests every day which means they had nine nights of practice, and that they stabilized by the fourth night. They were all relatively simple, easily learned tests--they were included for that reason. By the fourth night, which would be four hours of practice, they were stabilized. And the second thing is that this was counterbalance design. So any learning effects should be balanced out. In other words, the carbon monoxide was not always the last exposure.

DR. AZAR: I meant in looking and analyzing your data, did you negate the learning phase?

CAPTAIN O'DONNELL: Only to the point of assuring that there was a plateau prior to the exposure starting. In other words, we did look to the extent that we assured ourselves that the subject had plateaued in performance and that he was not continuing to learn before we started exposures.

DR. HODGE: If I understand, after the four nights of practice, which was uniform for all subjects, and thereafter some subjects had carbon monoxide the first night, some the second or third?

CAPTAIN O'DONNELL: Yes, there was completely random choice out of whatever method they chose to randomize so that, I forget the exact sequencing, but I think one subject had carbon monoxide on the first night, two subjects had a control on the first night, and it was completely random among the four subjects.

FROM THE FLOOR: What were smoking habits in the subjects?

CAPTAIN O'DONNELL: We assured ourselves because of some previous experience that none of the subjects were smokers, both by observation and by carboxyhemoglobin determinations under control conditions. We had one subject in the previous study that lied to us. We caught him on the carboxyhemoglobin.

DR. ROBERTSON (Hazleton Laboratories, Inc.): I wondered whether in addition to your scientific observations you made any notes on mood or such factors as impetuosity or clumsiness? Whether there is any change indicating loss of inhibition in subjects?

CAPTAIN O'DONNELL: We had the subjects fill out a questionnaire after each exposure and we also questioned them the night following each possible exposure as to their behavior during the day and we got absolutely no subjective response. There was no subjective ability to determine whether carbon monoxide was present, there were no consistent reports of any changes. Twice we thought we had beaten the double blind, since subjects reported that they went home and slept for three or four hours--two different subjects said this "I went home and slept today". And I thought, well this must be it, and they both turned out to be zero conditions. There was absolutely no correlation between subjective report and what we later found out to be CO exposure.

DR. HODGE: I remember you said in your checking of these average numbers that you found no statistical significance, even where there were consistent differences, always small, but always the same direction. Now did you do a sign test check on this, and was that not significant also?

CAPTAIN O'DONNELL: That's correct with one exception of the stage one sleep where we had eight positive changes. All of the apparent mean differences here were also checked nonparametrically and none of them was significant with that one exception.