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Trace Anesthetic Effects on Perceptual, Cognitive, and Motor Skills

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Forty male students were each exposed on two occasions to four hours of inhalation of either air or 500 ppm nitrous oxide with or without 15 ppm halothane in air. Immediately following exposure, a battery of tests of perceptual, cognitive and motor skills was administered. Compared with responses after breathing of air, those after exposure to nitrous oxide and halothane showed significant decrements in perfomances of a task in which attention was divided between auditory and visual signals, a visual tachistoscopic test, and memory tests involving digit span and recall of word pairs. Subjects exposed to nitrous oxide alone scored significantly lower on the digit-span test only. (Key words: Anesthetics, volatile: halothane; Anesthetics, gases: nitrous oxide; Psychologic function.)

THE MOTTO of the American Society of Anesthesiologists is "Vigilance." This quality is defined in Webster's New 20th Century Dictionary as "attention of the mind in discovering or guarding against danger or in providing for safety." With the large number of stimuli presented to the senses of the anesthetist, requiring his recognition of them (perception), decision-making (cognition) and action (motor activity), this byword is indeed appropriate. Anything which might impair these behavioral modalities could constitute a threat principally to the patient for whom the anesthetist provides care, and perhaps also to the anesthetist himself as he drives home and/or enters into other potentially hazardous activities following a working day. Anyone who has administered ether is aware that in an operating room not equipped for scavenging overflow vapors he absorbs an amount of this agent sufficient to be smelled on his breath. Despite the advent of agents more potent, and less easily detected by this means, we have shown that measurable amounts are present in end-expired air.[1] Corbett has studied breath decay curves for methoxyflurane and halothane and shown the persistence of these agents in the anesthetist for many hours following cessation of their use.[2]

We designed a study in which volunteer subjects were exposed for four hours either to air or to amounts of nitrous oxide with or without halothane in ambient concentrations comparable to those measured in our operating rooms before we began scavenging overflow anesthetics. Immediately following these exposures, they were subjected to several psychological performance tests. The results have important implications in clinical anesthesiology.

Methods

Forty paid volunteers were selected among dental and medical students at Northwestern University. Male subjects were chosen, to avoid any possibility of an effect of trace anesthetics on an early pregnancy in a female subject. Selection was limited to those not recently exposed to anesthetics either as patients or during clinical training. Each was interviewed to assure that he was in good general health, taking no prescription drugs, and understood the purpose of the study and agreed to it. Each individual signed an informed consent agreement to participate.

Each subject was assigned a day on which he would be tested at a given hour. He was then scheduled to be tested on the same day at the same hour a week later. On one of these days he was exposed to air, and on the other to the trace anesthetics and air. The

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TABLE 1. Sequence of Tests

Audiovisual task
Wechsler Memory Scale
Mental Control
Memory Passages
Visual Reproduction
Paired Associates
Tachistoscopic task
Wechsler Adult Intelligence Scale
Similarities
Digit Span
Digit Symbol
Picture Completion
Block Design
Picture Arrangement

order was counterbalanced so that half the subjects were tested first following exposure to air, and the other half first after receiving the trace anesthetics and air. During exposure, the subject was seated in a reclining chair, over which was suspended a standard hospital oxygen tent. The individual was not restricted in his movements within the tent, was free to read or do as he pleased, but was cautioned not to fall asleep. A flow rate of 70 pm of filtered, compressed air provided adequate ventilation, as determined both by the comfort of the subject reported to us and normal ambient O_2 and CO_2 values in samples obtained from the tent during the exposure. During the four hours the subject was seated in this situation, samples were taken periodically from a catheter inserted through the top of the tent and suspended within a few inches of his breathing zone.

The anesthetics were administered by adding a small amount of 1 per cent halothane in N_2, measured by metering, from a tank via a line of Teflon tubing to a larger Teflon line carrying the mainstream of air to the subject. Nitrous oxide was delivered from an anesthesia machine into a third line connecting to the line carrying the flow of air. The line carrying the resultant mixture passed over a screen, which prevented the subject from seeing the equipment, and was connected to the top of the tent. The flow rates of anesthetics were adjusted empirically to maintain concentrations within 10 per cent of the prescribed levels of 15 ppm for halothane and 500 ppm for N_2O, determined by gas chromatography. Our gas chromatograph is not sensitive enough to measure accurately end-expired concentrations in such subjects, so exposure was regulated only by carefully maintaining the desired levels of agents in the breathing zone of the subject.

At the end of four hours, the subject was taken immediately from the tent to a testing room across the hall; within 5 minutes testing was begun in the sequence shown in table 1. The audiovisual test involved perception of, and appropriate reaction to, independent changes in auditory and visual signals. The experimental equipment consisted of a two-channel oscilloscope (Hewlett-Packard), a four-channel FM instrumentation tape recorder (Hewlett-Packard), earphones to receive the auditory output from the recorder, and a response panel which was custom-made for this equipment. On the first two channels of the magnetic tape a pattern of ventricular fibrillation from a commercial electrocardiographic stimulator was recorded; on the fourth channel the clicking of a metronome at either 100 or 200 clicks per minute was recorded; on the third channel the responses of each subject as he pushed the appropriate button on the response panel were recorded. Figure 1 shows this equipment in use. The visual pattern was programmed to appear on either the bottom or the top channel of the oscilloscope. Thus, a two-by-two combination of conditions was presented to the subject as follows: visual high, sound slow; visual high, sound fast; visual low, sound slow; visual low, sound fast. On the response panel at the fingertips of the subject was one button for each of these four possibilities. As soon as he detected a change in either visual or auditory condition, he depressed the button corresponding to the new set of conditions. There were 100 changes programmed onto the tape (25 changes to each of the four conditions), and these occurred over a period of seven minutes, 20 seconds. By recording the responses of the subject on the empty channel of the tape, the test could be conducted quickly and the responses saved for grading after the subject had completed the other

FIG. 1. Volunteer seated at audiovisual test described in text. The tape recorder is sending auditory signals to the earphones and visual signals to the two-channel oscilloscope. The subject indicates recognition of a change in either mode by depressing the appropriate button on the response panel.

tests. At that time, the tape was played through a Grass polygraph recorder, which simultaneously printed out signals for visual and auditory patterns, plus the responses of the subject. From this written tracing, in which the changes in signals were clearly identifiable, the times taken for the recorded responses of the subject could be measured. Mean reaction time could thus be calculated from the time of stimulus change to the time of occurrence of the correct response. Pilot work had indicated that subjects averaged about 97 per cent correct on this task. A high level of correct responses is desirable for an accurate measure of reaction time.

Next, the subject was given psychological tests listed in table 1. Selected sections from the Wechsler Memory Scale, Forms I and II, were given first. Form I tests were always given during the first session. Mental Control involved counting backward, saying the alphabet rapidly, and tasks of that sort. Memory Passages was a test in which two paragraphs were read to the subject, his task being to remember as many "facts" as possible and to repeat them. Visual Reproduction involved the subject's drawing a picture that he had seen for ten seconds, following its removal. Paired Associates was a test in which the subject was to say the second member of a pair of words when the first one was given.

Next, the subject was seated in front of a tachistoscope. Looking into this instrument he viewed a square divided into nine small squares for 1/20th of a second. The small squares contained black circles which each time were varied in number (4, 5 or 6) and position. Fifteen such slides were seen, twice each, for a total of thirty presentations. The subject's task was to indicate on a grid comparable to the slide the location of the circles in each presentation.

TABLE 2. Tests Showing Significant Effects of Trace Amounts of Anesthetics*

Task	Significance
Audiovisual task	$P < .001$
Tachistoscopic task	$P < .025$
Memory Passages	$P < .05$
Digit Span	$P < .05$
Paired Associates	$.05 < P < .10$

* N_2O, 500 ppm; halothane, 15 ppm in air.

Following this, selected parts of the Wechsler Adult Intelligence Scale (WAIS) were given. Similarities was a task in which the subject was asked, "What makes these two words similar?" Digit Span was a task in which a series of numbers was recalled, both forward and backward. The Digit Symbol test involved giving the subject a written symbol for each of the digits, one through nine. His task was then to reproduce the correct symbol for each of a random array of these digits, with the tester recording the maximum score achieved in 90 seconds. Picture Completion was a test asking the subject to tell what was missing from a picture, *e.g.*, a United States flag with only 35 stars. Block Design involved reproducing pictures using blocks with three kinds of faces, some tasks using four blocks for 2 × 2 designs and some using nine blocks for 3 × 3 designs. Finally, Picture Arrangement involved arranging sets of pictures to make a logical story. The repeat tests, following the second exposure, used the identical tests for Similarities and Digit Symbols. For the other sections chosen from the WAIS, half of the items were utilized for each testing session. The entire test session took approximately 40 minutes to complete. Following this, the subject was allowed to leave the laboratory and the audiovisual test was recorded on paper by playing the tape through the polygraph as described. The results were tabulated later and the data subjected to statistical analysis, using analysis of variance to differentiate the statistical significance of anesthetic effect from the learning effect of improvement from the first to the second test session. An assessment of possible interaction of learning and anesthetic effect was also available by means of this analysis. Twenty subjects (Group I) were exposed to air containing halothane and nitrous oxide in the concentrations described; the other 20 subjects (Group II) received 500 ppm N_2O in air, and were tested identically.

Results

Group I subjects were asked to state whether they believed they were being exposed to the anesthetic or air condition on each exposure. Uniformly, they were unable to detect any difference in the odor of the air they were breathing, and the randomly correct answers given to this question were, by admission of the subjects themselves, strictly guesses. Of interest is the fact that in six of the 20 test situations in this group the subjects fell asleep spontaneously at some time during the 4-hour exposure; in all of these instances they were in the anesthetic-exposure condition. Even then, the subjects were unable to identify correctly this fact. None of these periods of sleep lasted more than 10 minutes, and each of the six subjects was awake and alert at the time of testing following exposure. The 20 subjects in Group II were studied following completion of study of those in Group I. They were also unable to identify the exposure conditions. The sleeping phenomenon was observed in two subjects in the N_2O condition, in the latter group, and in one in the control condition of exposure to air alone.

Those tests reaching statistical significance for anesthetic effect in Group I subjects are listed in table 2. The most striking decrement in performance produced by exposure to trace amounts of anesthetic was in the audiovisual task. Table 3 summarizes the Group I data from this task, giving the mean reaction times in the four conditions and indicating the effect of order of testing. Regardless of this order, mean reaction times increased by almost ½ second after exposure to traces of halothane and N_2O. Analysis of variance indicated statistical significance of the anesthetic effect beyond the .001 level. Neither the effect of learning nor the interaction of learning and anesthetic effect reached significance. Considering the other tests listed in table 2, statistically significant decrements in performance related to anesthetic exposure were also shown in the tachistoscopic task, Memory Passages and Digit Span. The decrement in the Paired Associates task was of borderline significance. Most of the Wechsler tests, of the type used in determination of I.Q., showed no significant difference.

For Group II subjects, exposed in the anesthetic condition to 500 ppm N_2O in air only, statistically significant anesthetic effects were, in general, not found. Neither the audiovisual nor the tachistoscopic task showed any effect, but the Digit Span test did show a significant effect of anesthesia, $P < .05$. As was true for the Group I subjects, the Paired Associates test in Group II also showed borderline significance of anesthetic effect ($.10 > P > .05$). Other than these, tests of Group II had negative results.

Discussion

Six of 20 subjects fell asleep sometime during the exposure to trace concentrations of halothane and N_2O, and two of 20 subjects breathing N_2O alone did the same. Only one of the 40 subjects slept while exposed to air alone. These observations, coupled with the objective findings of the psychological tests given immediately following exposure, suggest strongly that occupational exposure to trace amounts of anesthetics may compromise seriously the vigilance of the working anesthesiologist. If the tests had been given during exposure, instead of immediately afterwards, it is likely that even greater decrements in performance would have been demonstrated.

Group II subjects, who received only 500 ppm N_2O in air in their anesthetic-exposure condition, showed less effect from this treatment than did those receiving N_2O plus halothane, so it is likely that most of the decrement in the performance of Group I subjects was produced by halothane. We elected not to study an additional 20 subjects with halothane alone, in order to economize in both money and time. Halothane is rarely found as the sole agent contaminating operating room air, but many techniques currently

TABLE 3. Mean Reaction Times for the Audiovisual Task, Group I

Order of Exposure	Air	Air; N_2O, 500 ppm; Halothane, 15 ppm	
First	1.48 sec	1.81 sec	*Learning Effect*
Second	1.28 sec	1.67 sec	
	Anesthetic Effect		

in use employ N_2O as the only inhalation agent. It was therefore of interest to see how much effect this gas might have on the functions studied. Two of the tests did show an effect, so N_2O does not appear to be entirely without depressant action even at this low concentration, which is often exceeded in certain conditions or at certain times in the conduct of anesthesia.

We believe that our audiovisual task showed the greatest sensitivity for detection of subtle effects. The subjects in the study were told there would be changes in the pattern of signals in this test, and prior to the first exposure had been given a 3-minute trial run to acquaint them with the equipment and test method and to minimize the learning effect from the first to second testing. Thus, they were oriented toward the detection and rapid recognition of these changes in signal, yet Group I subjects had reaction times which were 150 per cent of their control values. This test situation differs from the clinical setting where the anesthesiologist is occasionally looking at an electrocardiographic monitor while listening with a stethoscope to heart sounds. In that case, his basic "set" is that everything is going along normally, with no significant change in signal from minute to minute. Changes from normal are relatively rare. Subjects removed from exposure to trace amounts of anesthetic were significantly slower in responding to changes they knew were coming and occurring every few seconds. It is possible that the clinician working in an unvented operating room might miss altogether a rare event such as a change in visual or auditory signal. If he were drowsy, this would be even more likely.

The tachistoscopic test, which also showed a significant decrement in the performance of Group I after exposure to anesthetics, was designed to resemble closely that used by Salvini and associates[3] for their studies of the effect of 110 ppm trichloroethylene on human subjects. Their study is of particular interest since trichloroethylene is still in use in clinical anesthesia and must be given in a high-flow system because of its incompatibility with soda lime. In practical terms, this results in a greater rate of escape of overflow gases into the operating room through various nonrebreathing valves. We have made only a few measurements of trichloroethylene in our operating rooms, since it is rarely used, but we found approximately 50 ppm in the ambient air near the anesthetist by the measurements we did make. This is not as high as the concentration reported by Salvini to have demonstrable depressant effects. However, we might expect that the effects found by them in an industrial setting might also hold true to some extent during our occupational exposure to this agent. Anesthetic contamination of operating room air may be reduced by simple means,[4] and this may be sufficient to eliminate any adverse effect of trace amounts of anesthetics on behavioral functions.

References

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Obstetrics

EPIDURAL ANESTHESIA FOR C SECTION Cardiac output, arterial pressure, blood volume, and total peripheral resistance were determined following continuous lumbar epidural anesthesia with carbocaine and no epinephrine in 13 normal-term pregnant candidates for repeat cesarean section. Cardiac output declined 6 per cent with the patient supine, rose 25 per cent in the immediate puerperium, and returned to preanesthesia values one hour after delivery. Heart rate remained constant, and total peripheral resistance declined by 229 dynes sec/5 cm when the abdomen was opened and returned to predelivery values one hour post partum. Central venous pressure rose from 4 mm Hg preoperatively to 8 mm Hg immediately following delivery.

Hemodynamic performance changed little after epidural anesthesia, in marked contrast to the changes found by these authors in the previous studies following both general and spinal anesthesia for cesarean section. Reasons for this difference are not immediately apparent. *(Ueland, K., and others: Cesarean Section under Epidural Anesthesia without Epinephrine. Am J Obstet Gynecol 114: 775–780, 1972.)*