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Laboratory Report

Psychological Studies of Human Performance as Affected by Traces of Enflurane and Nitrous Oxide

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Thirty human subjects were exposed for four hours to 500 ppm N_2O and 15 ppm enflurane in air and then, within five minutes, given a 35-minute battery of psychological tests. Performance of a divided-attention audiovisual task and a digit-span memory test were significantly decreased compared with control data following exposure to air. A tachistoscopic task, four tests from the Wechsler memory scale, and five others from the Wechsler Adult Intelligence Scale were unaffected. Thirty subjects exposed to 500 ppm N_2O in air only scored significantly lower on the digit-span test only. (Key words: Anesthetics, volatile, enflurane; Anesthetics, gases, nitrous oxide; Psychologic responses, trace anesthetics.)

IN A PREVIOUS REPORT,[1] we described decrements in performance of tasks measuring perceptual, cognitive and motor skills immediately following exposure for four hours to a combination of 15 ppm halothane and 500 ppm nitrous oxide (N_2O). Subjects exposed to N_2O alone scored significantly lower on the digit-span test only. Subjects exposed to the mixture of halothane and N_2O did significantly more poorly not only on that task, but also in an audiovisual reaction time test, a visual tachistoscopic test, and a memory test involving recall of word pairs. We thought it would be of interest to compare results with another volatile agent in combination with N_2O, and selected enflurane for this purpose. Results of tests given to human subjects so exposed, as well as an expanded study of those exposed to N_2O only, form the basis of this report.

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Methods

The exposure and testing procedures in this study were identical to those used previously with halothane and N_2O.[1] Thirty subjects were selected for exposure to 15 ppm enflurane and 500 ppm N_2O in combination in air, and ten more were exposed to 500 ppm N_2O in air only. The data from these ten were combined with those from 20 subjects in the previous study who were exposed to 500 ppm N_2O only. Thus, a total of 30 subjects for each of the anesthetic exposure conditions forms the data base for this study.

TABLE 1. Battery of Tests Administered

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

As in the previous study, all volunteers were male students in good health and taking no medication who signed a consent form and were paid to participate. Each subject was tested on two occasions, one week apart. During one four-hour exposure he breathed only air, and during the other he was exposed to the trace anesthetics in air. The orders of exposure were counterbalanced. In all anesthetic-exposure conditions, N_2O was maintained within 10 per cent of 500 ppm by measuring ambient samples of gas chromatographically and adjusting flow rates as needed. When enflurane was used, it was delivered from a tank of 1 per cent enflurane in N_2 and the concentration adjusted following appropriate measurements. Enflurane was also maintained within 10 per cent of the prescribed concentration of 15 ppm. Exposure was for four hours, at the end of which the subject was removed from the exposure tent and testing was immediately begun, as previously described.

The entire battery of tests is listed in table 1. Tests were begun within five minutes of the termination of anesthetic exposure and required approximately 35 minutes. The audiovisual test, in which performance would improve by practice gained following repeat administrations, was given to the subject for a three-minute practice session prior to the first exposure to either air or anesthetic. To assess the contributions made to differences in data by the factors of anesthetic exposure and this practice effect, the data were tabulated in a 2 × 2 design (table 2). In this way, an analysis of variance could be employed to analyze statistically the differences among the mean scores for the 15 subjects represented in each of cells A, B, C and D. The subjects are the same in cells A and D, and in cells B and C. Cross comparisons between any two cells are not made with this analysis, which takes into account all four means. Total variance among the four cells is partitioned into components coming from specific sources, and each is independently assessed for statistical significance.[2] In this way, anesthetic effect and practice effect are differentiated.

TABLE 2.

Exposure	Air	Air + Anesthetic
First	A	B
Second	C	D

If practice causes improved performance:
C will be better than A
D will be better than B

If anesthetic causes poorer performance:
A will be better than B
C will be better than D

If both are true, and anesthetic effect predominates:
C will be the best score
A will be next
D will be next
B will be the worst score

Results

The data from the 20 subjects exposed to air or 500 ppm N_2O, reported previously,[1] are included with the additional data provided by the ten subjects so exposed in this study. These ten subjects provided data which were comparable to those from the previous 20, allowing this pooling of data. The total group of 30 subjects is reported, together with an additional group of 30 who received either air or 15 ppm enflurane and 500 ppm N_2O in air.

In both groups of subjects, individuals were uniformly unable to detect whether they were being exposed to the anesthetic or air condition on each exposure. Three of the 30 subjects exposed to N_2O alone, and two of the 30 exposed also to enflurane, fell asleep during the four-hour exposure. An additional subject fell asleep during exposure to air alone but not during subsequent exposure to 500 ppm N_2O in air.

The only significant decrements in performance of these tests were those noted with the audiovisual task and the digit-span test. Nitrous oxide alone affected only the digit-span test, but when combined with enflurane lowered performances on both this and the audiovisual task. The mean reaction times, and numbers of digits recalled, respectively, for these two tasks are given in tables 3 and 4 for those exposed to N_2O

TABLE 3. Audiovisual Task, Mean Reaction Time in Seconds

Exposure	Air	Air + 500 ppm N_2O
First	1.47	1.60
Second	1.32	1.21

Significance of anesthetic effect: P = N.S.
Significance of practice effect: $P < 0.025$.

TABLE 4. Digit-span Task, Mean Number of Digits Recalled

Exposure	Air	Air + 500 ppm N_2O
First	16.3	14.9
Second	15.9	14.6

Significance of anesthetic effect: $P < 0.05$.
Significance of practice effect: P = N.S.

TABLE 5. Audiovisual Task, Mean Reaction Time in Seconds

Exposure	Air	Air + 500 ppm N_2O + 15 ppm Enflurane
First	1.33	1.35
Second	1.19	1.34

Significance of anesthetic effect: $P < 0.005$.
Significance of practice effect: P = N.S.

TABLE 6. Digit-span Task, Mean Number of Digits Recalled

Exposure	Air	Air + 500 ppm N_2O + 15 ppm Enflurane
First	13.6	13.1
Second	14.4	13.5

Significance of anesthetic effect: $P < 0.05$.
Significance of practice effect: P = N.S.

only and in tables 5 and 6 for the experiments employing a mixture of N_2O and enflurane. The statistical significance of anesthetic effect, derived from an analysis of variance, is listed with each table. The effect of practice was not significant except for subjects exposed to N_2O only who were given the audiovisual task (table 3).

Discussion

The principal findings of this study were that enflurane affected performance on these tests in a manner qualitatively similar to, though quantitatively different from, halothane. Since the minimum alveolar concentration (MAC), an index of anesthetic potency, is about twice as high for enflurane as for halothane, comparison of the same trace amounts of each agent would be expected to show a smaller effect of enflurane. This was found in these studies. In addition, the end-expired concentration of enflurane following cessation of anesthetic administration decreases at approximately twice the rate of halothane in the amount of time taken for these tests.[3] Despite these limitations, statistically significant impairment of performance of subjects was produced by enflurane, as well as by 500 ppm N_2O when given as the only anesthetic. These findings confirm the previous conclusion that trace anesthetic concentrations in amounts found in operating rooms not specially equipped for elimination of overflow anesthetic gases may interfere with optimum performance on psychological tests measuring perceptual, cognitive and motor skills. The anesthetics were being cleared from the subjects even as they were being tested, so if they had been tested while being exposed, performance decrements would probably have been even greater.

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