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The Anesthetic Effect of Air at Atmospheric Pressure

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Nitrogen has recognized narcotic potential at hyperbaric pressures. No narcotic effect of helium has been demonstrated at any pressure. We evaluated the effect of nitrogen in air at one atmosphere on human performance by comparing it with helium–oxygen using a four-alternative divided-attention task that requires rapid response to auditory and visual signal changes. There was a 9.3 per cent decrease in response time when subjects breathed helium–oxygen, a significant change ($P < 0.001$). This change could not be ascribed to practice since the order of presentation of gases did not have a significant effect. It is concluded that the nitrogen in ambient air slightly but measurably impairs human performance compared with a non-anesthetic gas such as helium. (Key words: Gases, non-anesthetic, nitrogen; Brain, psychomotor function, nitrogen.)

TRACE CONCENTRATIONS of anesthetic agents ($5–19 \times 10^{-4}$ MAC) measurably decrease performance in human volunteers.[1] The demonstration of effects from such small concentrations led us to ask whether air at ambient pressure might also exert a narcotic effect. It is known that anesthetic potency is directly related to lipid solubility.[2] For man, this relationship is described by: MAC × oil/gas partition coefficient = 1.4.[3] MAC is defined as "the minimum alveolar concentration of anesthetic at one atmosphere that produces immobility in 50 per cent of those patients or animals exposed to a noxious stimulus."[3] The oil/gas partition coefficient for N_2 (0.074) gives a predicted MAC of 18.9 atmospheres absolute. Thus, the N_2 content of air at ambient pressure equals 4.24×10^{-2} MAC, a far higher concentration than that used by Bruce *et al.*[1] in their studies of the effects of trace anesthetic concentrations.

Basing our study on these theoretical and experimental considerations, we evaluated the effect of ambient nitrogen by comparing, in human volunteers, air with 79 per cent helium in oxygen. The low oil/gas partition coefficient for He (0.017) gives a predicted MAC of 82.4 atm abs, but no anesthetic effect of He has been demonstrated, presumably because of pressure antagonism of narcosis. Therefore, substitution of He for N_2 should unmask any anesthetic properties of air.

Methods

Twenty young healthy volunteers of both sexes were informed of the nature, but not the purpose, of the experiment. Each was determined to be in good health, and selection was limited to those having no recent exposure to anesthetic agents or prescription drugs. Subjects were instructed not to indulge in alcohol or other psychoactive or depressant drugs for a week prior to the study. One subject was refused participation for lack of adherence to these instructions. A second was eliminated due to a temporary equipment failure. All subjects signed an informed consent to participate. Performance was evaluated using an audiovisual task sufficiently sensitive to detect performance

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decrements following inhalation of trace concentrations of anesthetics.[1] Requirements of the test were that it be highly sensitive and easily learned. A dual-modality divided-attention task was chosen because this type of test has been shown to fulfill those specifications.[4]

A four-channel FM instrumentation tape recorder (Hewlett-Packard, Model 3960) was used to record and play back auditory and visual signals. The visual portion was a ventricular fibrillation pattern generated by an ECG simulator (Hewlett-Packard, Model 4653B). This was played back through a two-channel oscilloscope, appearing alternately and at irregular intervals on the upper and lower channels. Simultaneously, auditory signals generated by a metronome were carried on the tape at speeds of 100 or 200 beats per minute, an easily recognizable difference. Subjects monitored the auditory signals by headphones. Stimulus combinations of visual high (upper channel), sound fast; visual high, sound low; visual low (lower channel), sound fast; and visual low, sound slow were presented, with 102 changes occurring in a 7.3-minute tape segment. Subjects were instructed to respond by pushing one of four buttons for the appropriate combination as promptly as possible after detection of either audio or visual signal change. Responses were recorded on the original tape and data transferred to paper via a Grass Model 7 polygraph for subsequent analysis.

Subjects were given two five-minute training sessions prior to the first exposure. Pilot work indicated that this was sufficient to learn the test to near maximum. However, a true performance plateau was not essential for these manipulations, since exposure to the two gases were counterbalanced; *i.e.*, half the subjects received He/O_2 first and air second, while the other half received the two gases in the alternate order. Additionally, statistical procedures employed allowed separate assessment of practice effect and change in performance due to inhalation of the gases.

Test gases were air and 21 per cent oxygen in helium, contained in covered cylinders.

TABLE 1. Response Times (Seconds)

	He/O_2	Air
Administered first	0.99 n = 9	1.12 n = 9
Administered second	0.95 n = 9	1.02 n = 9
Overall mean ± SD	0.97 ± 0.14	1.07 ± 0.15

TABLE 2. Analysis of Variance

Source	SS	df	MS	F
Order (gas)	.045	1	.045	1.15†
Error	.631	16	.039	
Nitrogen	.084	1	.084	21.00*
Order N_2	.011	1	.011	2.75†
Error	.062	16	.004	
TOTAL	.833	35		

* $P < 0.001$.
† Not significant.

They were delivered to a standard anesthetic circle with CO_2 absorber at an inflow rate of 10 l/min, and were breathed by subjects via a carefully fitted face mask. Composition of respiratory gases was monitored continuously for N_2 in the expiratory line with a Warren E. Collins, Inc. fast-response N_2 analyzer, and intermittently from the inspired limb for O_2 and CO_2 by standard techniques.

Because of voice distortion produced by He, subjects were requested not to vocalize during mask breathing. Subsequent questioning confirmed that they were unable to determine which gas was being delivered at a given time.

Subjects equilibrated with the first gas for 20 minutes, then took the 7.3-minute test. Thereafter, gases were switched, a further 20-minute equilibration allowed, and the test repeated. Inspired O_2 was 20–21 per cent and CO_2 unmeasurable (less than 1 torr). Nitrogen in expired gas decreased promptly and remained below 3 per cent after 5 minutes of helium breathing, except for two cases of brief transient N_2 contamination due to momentary breaks in the mask seal.

Data were analyzed for stimulus response time and number of errors, and subjected to analysis of variance.

Results

Sixteen of the 18 subjects tested responded more rapidly when breathing helium–oxygen than when breathing air. These data are presented in table 1. Accuracy was consistently greater than 97 per cent under all conditions.

As may be seen in table 1, there was a 9.3 per cent mean improvement in response time during the helium–oxygen breathing. Table 2 indicates that this was the case regardless of the order of presentation of gases. Analysis of variance indicated that it represents a highly significant increment in performance, $F(1,16) = 21.00$, $P < 0.001$. Neither the effect of practice nor the practice order × exposure condition reached significance in this analysis (table 2).

Discussion

Although compressed-air narcosis at hyperbaric pressure has been known since the nineteenth century,[5] it was not until 1935 that Behnke, Thomson and Motley[6] demonstrated that it was caused by the increased partial pressure of N_2. The Meyer-Overton hypothesis,[7] which correlates lipid–gas partition coefficients with anesthetic potency, gives a calculated MAC for N_2 of 18.9 atm, or 23.6 atm of air. MAC for N_2 is considerably higher than this predicted value in dogs (>43 atm)[2] or mice (33 atm).[8] The explanation for the discrepancy lies partially in the antianesthetic effect of increased hydrostatic pressure,[9] and partly in the lower MAC values generally found in man as opposed to other animals.[3]

That N_2 in air at atmospheric pressure might cause a subliminal but measurable anesthetic effect was suggested by Miles[10] but, prior to these studies, has not been demonstrated. Dunn[11] found no significant increment of psychomotor function of volunteers in the presence of decreased N_2. However, our results are not unexpected in view of the investigations of Bruce *et al.*, who demonstrated the effects of 15 ppm halothane and 100 ppm N_2O,[1] and 15 ppm of enflurane, on response time utilizing the same test we employed in the present study. Performance decreased significantly at concentrations of halothane–N_2O or enflurane that were two orders of magnitude less than the calculated fraction of MAC for N_2 in atmospheric air.

We have ascribed the more rapid response seen with helium to the removal of nitrogen from the breathing mixture. An alternative explanation might be a hitherto unknown stimulant effect of helium. Data to refute or support this alternative are limited. It is known that extremely high helium (and hydrogen) pressures produce hyperexcitability and convulsions in animals, but these effects have been convincingly attributed to increased barometric pressure, rather than the gases inspired.[12]

Both theories of anesthetic action and the evidence cited in this report suggest that the nitrogen concentration in atmospheric air causes a measurable performance decrement in man, that the "nitrogen blanket" effect suggested by Miles[10] is a real phenomenon, and that human history has proceeded under partial narcosis. Perhaps this explains the current state of world affairs.

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Neonatology

OXYTOCIN CHALLENGE It has been suggested that applying standard stress with oxytocin during the antenatal period may be of use in assessing fetal well-being or the ability of the fetus to withstand labor. The oxytocin challenge test was applied to a group of 50 high-risk obstetric patients, and the results were correlated with urinary estriol, the occurrence of fetal distress in labor, Apgar score, and high-risk index. Thirty-five patients had negative tests, nine had positive tests, and six had only unsatisfactory tests. There was no correlation between a positive test and low estriol level, the occurrence of fetal distress in labor, or Apgar score. However, the results suggest that a negative test in a high-risk pregnancy may indicate that the pregnancy should be allowed to continue. *(Christie, G. B., and Cudmore, D. W.: The Oxytocin Challenge Test, Am J Obstet Gynecol 118:327–330, (February 1) 1974.)*

RITODRINE EFFECTS ON MOTHER AND FETUS The effects of administration of ritodrine hydrochloride (150 μg/min) on uterine activity and maternal and fetal cardiovascular status were evaluated in ten patients in active labor.

Ritodrine infusion resulted in a marked decrease in uterine activity and increase in maternal pulse rate (40 beats/min), with minimal increase in pulse pressure. These changes were maximal 30 minutes after the start of infusion. Maternal tachycardia persisted after discontinuation of the drug. Nonspecific ECG changes were considered to be rate-related. Ritodrine caused no change in the fetal heart rate, ECG, or acid–base status. *(Nichimson, D. J., and others: The Effects of Ritodrine Hydrochloride on Uterine Activity and the Cardiovascular System, Am J Obstet Gynecol 118:523–528, 1974.)*

BLOOD VOLUMES OF INFANTS BORN BY CESAREAN SECTION The total blood, plasma and erythrocyte volumes of 23 term neonates born by cesarean section were studied with respect to time of cord clamping and position of the infant. Immediate clamping at the level of the uterus resulted in blood volume comparable to that previously reported for the term fetus born after vaginal delivery (87 ml/kg). Delayed clamping of the cord (3 minutes postpartum) with the infant held 15 cm above the uterus caused a significant reduction in blood volumes (67 ml/kg). In contrast, delayed clamping with the infant placed 15 cm below the uterus resulted in increased volume (106 ml/kg). *Sisson, T. R. C., and others: The blood volume of infants. IV. Infants born by cesarean section. Am J Obstet Gynecol 117:351–357, 1973.)*