

Inhalation Of Nitrous Oxide Decreases Olfactory Performance

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Citation

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Abstract

Study objective: Studies with volunteers breathing volatile agents and nitrous oxide have demonstrated an altered sensorium, but none has specifically addressed the issue of olfaction. Since nitrous oxide is odorless, well tolerated, and has been shown to alter the sensorium, this study was designed to examine the effect of nitrous oxide on olfaction.

Design: Prospective randomized volunteer study.

Setting: Anesthesia simulator laboratory at the University of South Florida.

Patients: 17 consenting adult volunteers were studied.

Interventions: Healthy volunteers were asked to describe five scents while breathing room air: coffee, bubblegum, wintergreen, sevoflurane, and ammonia. They were then asked to again identify the scents while breathing nitrous oxide at end tidal concentrations of 30%, 40%, 50%, 60%, and 70%.

Measurements: All patients were monitored for blood pressure, pulse oximetry, end-tidal carbon dioxide concentration, end-tidal nitrous concentration, and heart rate. Scents were introduced at each level of nitrous oxide in a random fashion.

Main Results: All subjects had increasing difficulty identifying the five scents with progressive levels of nitrous oxide inhalation. Even those scents identified correctly were described as being less intense, and in the case of ammonia, more tolerable. Hemodynamic stability was maintained, and all subjects remained conscious at all times.

Conclusions: Nitrous oxide blunts olfaction in a dose dependent fashion. Breathing nitrous oxide prior to inhalation induction with a volatile agent may render inhalation induction less unpleasant and make it a more tolerable option for certain patients.

INTRODUCTION

Despite the widespread use of inhalation induction of anesthesia in children, adult inhalation inductions have not become as popular or prevalent. ¹ This practice is in part due to the perception that patients find mask induction unpleasant, because of the pungent odor of volatile anesthetics. Even sevoflurane, considered to be the least pungent of the volatile agents, is regarded as extremely unpleasant by some patients during inhalation induction.

Inhalation induction has a number of potential uses and benefits. First, patients in whom apnea or muscle relaxation are contraindicated (such as patients with epiglottitis)

maintain spontaneous ventilation with inhalation better than during intravenous (IV) induction of anesthesia. Second, it has been reported that hemodynamic lability is less severe with inhalation versus IV induction.¹ Finally, some patients either present a significant challenge in IV catheter insertion, or have 'needle phobias'. Both of these groups of patients are frequently more-than-willing to forego multiple attempts at IV access, and prefer inhalation induction.

Nitrous oxide (N₂O) is an odorless gas often used to speed onset of anesthesia, augment volatile anesthetics, or provide sedation in awake patients. Studies with volunteers breathing N₂O and volatile agents have demonstrated an altered

sensorium, but none have addressed the issue of olfaction.^{2,3} Since N₂O is odorless, well tolerated, and alters the sensorium, this study was designed to examine the effect of N₂O on olfaction.

METHODS AND MATERIALS

Following institutional review board approval of the research protocol, 17 consenting adults were brought to the University of South Florida simulator laboratory. Exclusion criteria included impaired olfaction secondary to upper respiratory infection, history of adverse reactions to N₂O, or pregnancy. Following a brief history and physical examination, standard ASA monitors were applied, and baseline heart rate, blood pressure, and pulse oximetry data were obtained.

The volunteers were exposed to and asked to describe five scents while breathing room air: coffee, bubblegum, wintergreen, sevoflurane, and ammonia. Each was introduced via a saturated cotton-tipped applicator placed briefly below the nostrils, and subjects were asked to sniff naturally.⁴ For sevoflurane, the subjects were asked to describe the scent, and then asked to use the same one-to-two word description during the study. They were then again asked to identify the scents while breathing N₂O at stable end tidal concentrations of 30%, 40%, 50%, 60%, and 70%. All subjects were monitored for blood pressure, pulse oximetry, end-tidal carbon dioxide concentration, end-tidal nitrous concentration, and heart rate. Scents were introduced at each level of N₂O in a random fashion. Randomization was achieved by computer program (Version 6.12, SAS Institute, Inc., Cary, NC).

Following completion of data acquisition, all subjects were asked to remain in the simulator laboratory until they felt completely comfortable and had achieved an Aldrete score of 10. Subjects were reimbursed \$50 for time spent in the study.

Statistical analysis: Kolmogorov-Smirnov test was used to examine the relationship between smoking history and scent detection. Ages were stratified into decades and dummy coded. Relationship between age and scent detection was assessed using Kruskal-Wallis ANOVA by Ranks.

RESULTS

Of the 17 participants, 15 were men, 2 were women. Three had a history of smoking, with only one being an active smoker. None had upper respiratory infections, allergic rhinitis, or a history of adverse reactions to nitrous oxide.

Mean age was 40±9 years. Three of 16 participants acknowledged varied histories of smoking. Scent detection was not influenced significantly by either age or history of smoking.

Variables reflecting cardiovascular function and oxygenation remained stable in all patients throughout the study and are summarized in Table 1.

Figure 1

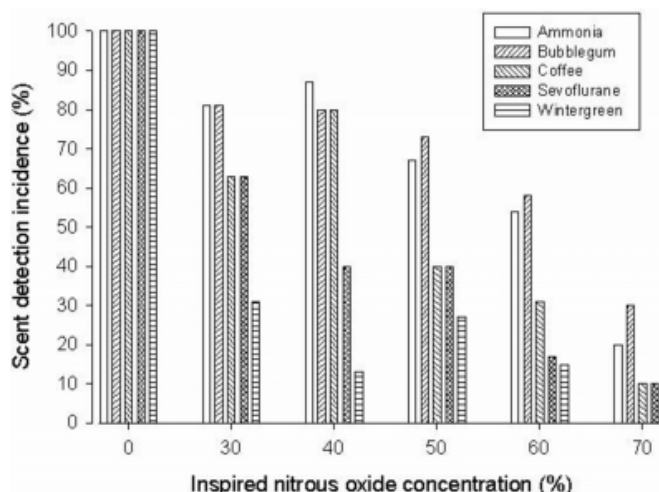
Table 1: Variables reflecting cardiovascular function during varied levels of inspired nitrous oxide. Data are presented as mean±SD.

	Nitrous oxide (%)					
	0	30	40	50	60	70
Participants (n)	16	16	16	14	11	7
Heart Rate (/min)	76±9	73±9	72±9	74±10	75±16	68±13
Systolic blood pressure (mmHg)	143±13	140±18	137±17	136±17	138±16	132±18
Diastolic blood pressure (mmHg)	82±8	82±11	83±9	83±9	86±12	85±12

All participants had progressive difficulty identifying the five scents with increasing levels of N₂O inhalation (Figure 1). Even those scents identified correctly were described as being much less intense at the 30% N₂O level, and, in the case of ammonia, more tolerable. Of note, 90% of subjects spontaneously identified sevoflurane as 'shoe polish' when asked "what does this smell like?"

Figure 2

Figure 1: Scent detection incidence at varying levels of inspired N₂O concentration. n=17.



DISCUSSION

Results of this study indicate that N₂O blunts olfaction in a dose dependent fashion. Potential benefits of this finding are that N₂O could be used to blunt the odor of volatile agents during inhalation induction in children and adults.

As previously stated, inhalation inductions at times are preferred, and desirable. Unfortunately, even those volatile anesthetics considered to be least pungent are still perceived as unpleasant.

Odors, more appropriately called odorants, are volatile chemical compounds that are carried by inhaled air to the olfactory epithelium, located in the roof of the nasal cavities. Odorant must have some water solubility, a sufficiently high vapor pressure, low polarity, and some lipid solubility.

The olfactory region of each of the two nasal passages in humans is a small area of about 2.5 centimeters square containing approximately 50 million sensory receptor cells.^{5,6} It consists of cilia projecting down out of the olfactory epithelium into the mucous layer. The mucous lipids assist in transporting the odorant molecules to the actual receptors in the olfactory cilia. The olfactory cilia are the initiation point for the molecular reception of the odorant and the beginning of sensory transduction.

Binding of odorants to cilia and activation of olfactory receptors occurs via G-protein coupled receptors, which stimulate adenylate cyclase, and open cAMP gated Ca⁺ channels. The signals are carried ipsilaterally within the olfactory bulb, through the lateral olfactory tract, and to higher centers in the brain where the signaling process is decoded and olfactory interpretation and response occurs.⁵

Also involved in the perception of inhaled chemicals is the trigeminal chemosensory system. Nociceptive neurons of cranial nerve V are activated by chemicals classified as irritants. Many of these irritants (such as ammonia, capsaicin) can also be recognized by the olfactory system as odorants, although the concentrations needed to activate the nociceptive receptors are usually much higher.⁶

Finally, the senses of smell and taste are complementary, and there is evidence of significant ties between olfaction and the limbic system, as demonstrated by the interactions of memory, emotion, and olfaction.

Limitations of this study include a limited number of tested odors, and a relatively small sample size. Also, the issue of irritant vs. odorant was not addressed. The threshold concentration of odorant to irritant for ammonia should be considered. Children could conceivably also be tested, but we felt that adult subjects would be a good starting point for this area of research. Future studies should focus on alterations of other senses, including vision and hearing, both of which seemed to be significantly affected in our

subjects. Additional consideration should be given to the observation that at high inspired N₂O concentrations, all subjects experienced some level of euphoria. There might be an inspired N₂O concentration at which patients are no longer aware or concerned about smells.

CONCLUSIONS

In conclusion, breathing N₂O prior to inhalation induction with a volatile agent, even at a relatively low inspired concentration, may render inhalation induction less unpleasant and make it a more tolerable option for certain patients.

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