

Nitrous Oxide: It's a Gas

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INTRODUCTION

It was Sir Humphry Davy who not only encouraged the use of nitrous oxide as an anesthetic and analgesic agent but also indicated its euphoric and pleasurable effects. In his treatise on the subject he indicated giddiness similar to alcoholic intoxication (p. 271), pleasurable thrilling in the chest and extremities (p272), and auditory and visual distortions (p. 272 and274). He introduced many friends and colleagues to the experience and implied that he was 'turned on' by the gas by noting, “. . . I continued occasionally to breathe the gas, either for the sake of enjoyment, or with a view of ascertaining its operation under particular circumstances" (p. 276). He added that there were no adverse effects on sleep (p. 274), or appetite (p. 271) and suggested a 'reverse tolerance' to the pleasurable effects by observing a greater effect with subsequent trials of the same amount of the gas (p. 285, 291).

Davy's impact on others is suggested by a proposal in the early 1800's for a nitrous oxide tavern reported by Agnew who quotes from a book entitled Chemical Experimentalist "In short, it is a clearly, time-saving exhilarating, angelizing ether; whereas spirituous liquors are besotting, brutalizing, devil-inspiring draughts which in the end clog the ideas, whereas the ethereal oxide sets them free."

Lingeman³ in his drug dictionary (p. 183) notes that the use of N₂O for its mind-altering effects is usually occasional and "undoubtedly harmless."

The physical qualities of N₂O are that it is a colorless gas with a sweet odor, that it is heavier than air and non-flammable. Nearly all-adverse effects are due to anoxia and not the gas itself. Its most serious direct physical effect is a slight depression of myocardial contractility. It has low anesthetic potency and cannot, by itself, carry an individual beyond plane II of anesthesia (pp. 71-73).⁴

NON MEDICAL USE OF N₂O

N₂O was used commercially for the first time in 1869 to aerate or effervesce drinks and since then has been used to effervesce heavy cream and other dairy products, to fluff ice cream, to whip cream, experimentally as a closed cycle refrigerant, as the first throwaway aerosol vehicle, in non food aerosols, as a leak detector and in ethyl ether motor starters. In 1845 an exhibition was held in the United States inviting the public to experience nitrous oxide and “. . . laugh, sing, dance, speak or fight, etc." There have been few reports about its use since. Dillon reported an auto accident of an individual under the influence of N₂O. Danto, on the other hand, reported an experience of laughter, increased excitement and no ill effects.

Objective studies by Parkhouse et al. concluded that you cannot get analgesia without some mental impairment and that both the effects of analgesia and mental impairment vary from subject to subject.

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Westerlund and his co-investigators following on Davy's statement that hearing was more acute after breathing the gas felt that there was no objective evidence for improvement and suggested that auditory hallucinations, preservation, positive after image or tinnitus may be involved rather than increased acuity.

Robson et al.¹⁰ noted that subjects under the influence of N₂O learned more slowly than controls but Frankenhaeuserl at lower concentrations found some improvement. Steinberg and Summerfield concluded that nitrous oxide retarded the formation of associations and interfered with the organization of serial tasks. Effects on recall, however, were slight. In an earlier study Steinberg showed that performance suffered most when subjects were given more complex tasks. All of the studies cited employed the use of nitrous oxide-oxygen mixes in laboratory settings with operating room set-ups and did not approximate the natural, non-medical use of the drug.

There have been an increasing number of anecdotal reports on the non-medical use of nitrous oxide. A research team of members of the departments of Psychiatry, Psychology, the Counseling Center and the Drug Education Project of Michigan State University, the Drug Education Center of East Lansing and the Governor's Office of Drug Abuse was organized to look at several aspects of the nitrous oxide scene.

METHOD

Survey.—Members of the Drug Information Center of East Lansing informally surveyed the "drug scene" to determine if and how N₂O was being used, and if its use was increasing.

Pilot Study.—Ten volunteers were used to establish a safe method approximating the natural use of the drug. The group consisted of 7 men and 3 women ranging in age from 21 to 42. Five of the subjects (Ss) had no previous drug experience save alcohol or prescription drugs ('straights') and five of the Ss had prior drug experience including marijuana, LSD, mescaline, heroin and others ('freaks').

All of the Ss were given complete physical and neurological examinations and hematocrit determinations were made. Ss were ruled out of the study if there was any evidence of cardiac, respiratory, neurologic or hematologic problems. Balloons were filled with pure N₂O and the Ss were asked to take as deep a breath as possible and to hold it for varying periods of time. Rebreathing the gas from the balloon was also employed. The time it took for a 'high' to be achieved was recorded, as were the Ss' remarks about the experience.

Objective and Subjective Study.—Three tests were utilized to assess cognitive functioning before, during, and at 5 and 10 minute periods after the onset of the N₂O effects.

The digit symbol test was taken directly from the Wechsler Adult Intelligence Scale. The task in the DS is to identify numbers by symbols according to a key; parallel forms were constructed by re-ordering the symbols in the key as well as the numbers in the body of the test.

The second test, developed by Norrell, was the symbol analogies test (SA) wherein the task is to identify the one geometric figure out of a set of figures that does not belong. Each item consists of 5 figures of 3 types (circle, square, or triangle) and the discrimination is made on a comparison according to figure type, size, shading, or all three variables in combination. Two parallel forms were made available and a third was constructed by selecting alternate items from forms 1 and 2.

The addition test (AD) consisted of 10 problems of randomly selected, four row - two column numbers. Parallel forms were arranged by reordering the numbers.

The Ss were 12 men and 12 women ranging in age from 19 to 30 with a mean age of 24.0. Based on their drug usage history Ss were assigned to either a drug naive group—straight (no previous history of drug use with the exception of alcohol and medically prescribed drugs) or a drug sophisticated group—freak (regular use of drugs for other than medical reasons). Each group contained 6 men and 6 women. None of the Ss had previous experience

with nitrous oxide. A biographical survey, designed to briefly assess the medical, psychological, and drug usage history, was completed by all Ss prior to testing.

There were four periods of test administration: Pre-test; Session 1 (during a high); Session 2 (5 minutes after inhalation); and Session 3 (10 minutes after inhalation). Because of scheduling difficulties four Ss sessions ranged from 30 minutes to five hours apart. For the remainder of the Ss the sessions were scheduled at 24-hour intervals. All Ss were instructed to refrain from drug usage for 24 hours prior to each session. All tests in all sessions were administered with a one-minute time limit.

On Pre-test day, following the completion of the biographical survey, a group administration of parallel form 1 of all 3 tests was accomplished. The Ss were then advised as to the safety and possible dangers of nitrous oxide inhalation and each subject was given one balloon-full (approximately 2 quarts) of pure N₂O. They were instructed to exhale all the air from their lungs, then to take a deep breath of the gas and to hold the breath as long as they desired. Following this initial introduction to N₂O the Ss completed an open-ended questionnaire describing their subjective experience with the gas.

In session 1 each S was individually tested in the following manner S was instructed to inhale one full breath of N₂O from a balloon and to hold the breath as long as he desired; 30 seconds after the initiation of inhalation (which had been previously determined to be within range of peak effect) the first test was administered (Post-high); 5 minutes after initiation of inhalation the second test was administered (Post-5); and 10 minutes after initiation of inhalation the third test was administered (Post-10). Parallel form 2 of all 3 tests was used in session 1.

In sessions 2 and 3 the procedure was identical to that of session 1 except that in session 2 parallel form 3 was used while in session 3 parallel form 1 was re-used.

The test type (DS, AD, SA), session number (1, 2, 3) and the temporal order of administration (Post-high, Post-5, Post-10) were completely counterbalanced so that all Ss received all 3 tests in all 3 temporal orders, and so that on any given day 2 subjects in each group (straight, freak) received the same test and temporal order.

Upon the completion of testing in session 3 all Ss were given a balloon-full of N₂O to breathe, as they desired. Following this they completed a semi-structured questionnaire concerning their subjective experiences with the N₂O. They were asked about anticipation, drug effects, adverse reactions, residual effects, beneficial effects, motivation, and whether or not they would be willing to participate in further research using nitrous oxide.

Scoring was accomplished by hand and was recorded in terms of the number correct and the number tried. The data were subjected to an analysis of variance.

RESULTS

Survey.—From the casual reports concerning the nitrous scene in mid-Michigan one would conclude that the use of the gas is by no means rampant but that its use has been increasing.

It was not uncommon to hear from individuals who had been to parties where a professional (doctor, nurse, dentist, inhalation therapist, researcher) had provided nitrous oxide. There also were those who work in restaurants who used the N₂O stored in tanks for the preparation of whip cream. Reports were received from

TABLE 1
MEAN CORRECT SCORE ON COGNITIVE TESTS
SA = SYMBOL ANALOGIES; DS = DIGIT SYMBOLS; AD = ADDITION

Subject	PreTest			High			5 minutes			10 minutes		
	SA	DS	AD	SA	DS	AD	SA	DS	AD	SA	DS	
AD												
Group	P	P	P	H	H	H	5	5	5	10	10	10

Male											
Straight (6)	6.00	44.5	6.67	6.33	34.7	5.17	7.00	45.3	7.17	6.30	
43.8	6.17										
Female											
Straight (6)	8.33	49.5	7.00	9.33	47.7	5.67	9.17	51.2	6.67	9.00	
50.2	6.83										
Total											
Straight (12)	7.17	47.7	6.83	7.83	41.2	5.42	8.08	48.3	6.92	7.67	
46.8	6.50										
Male											
Freak (6)	9.67	44.0	8.00	9.50	27.8	5.33	10.3	44.8	8.17	10.0	
45.8	7.50										
Female											
Freak (6)	10.5	46.2	6.83	9.83	40.3	4.83	11.2	46.3	6.67	11.7	
49.3	6.50										
Total											
Freak (12)	10.1	45.1	7.42	9.67	34.1	5.08	10.8	45.6	7.42	10.8	
47.6	7.00										
Total	8.62	46.0	7.13	8.75	37.6	5.25	9.42	46.9	7.17	9.25	
47.2	6.75										
Subjects (24)											

individuals who used the gas contained in aerosol cans both of food and non-food products. At a recent rock festival nitrous oxide was widely sold for 25 cents a balloon. Contact was made with a "mystical-religious" group that used the gas to accelerate arriving at their transcendental-meditative state of choice. Although a few more sophisticated users employed nitrous oxide oxygen mixes with elaborate equipment most users employed balloons or plastic bags. They either held a breath of N₂O or rebreathed the gas. There were no adverse effects reported in the more than one hundred individuals surveyed.

Pilot Study.—All of the 10 subjects signaled a high at from 15 to 30 seconds. The initial peak effects lasted for about 2 to 3 minutes and were described as pleasurable by all. One S described the effect as a "mentholated stone" explaining that it was a higher high than marijuana but much cooler. All described a "head rush" perceiving tingling or warmth around the face and head and auditory illusory or hallucinatory phenomena. Rebreathing the gas from the balloon prolonged the peak high. Although the peak effects dissipated in a few minutes, all the Ss described a state of well being that lasted from 30 minutes to several hours after the experience. All described more intense and prolonged experiences with subsequent trials using the same dosage. Several volunteered that headache; shoulder pain and mild depressions were ameliorated during the experience and did not return. One of the straight Ss (age 36) reported:

I seem to reach the high point within seconds. I felt my face become flush as though all the blood in my body suddenly rushed up to my head. The warmth in my face was similar to the feeling I get when I drink an alcoholic beverage, except at a much slower rate. After reaching the high point the down period felt as though there was some regulator e.g. tourniquet, around my neck which let the drops of blood from my head pass to the rest of my body at an accelerating rate (very slow at first i.e. drop by drop then a steady stream). This was the internal feeling external feeling of the down period was like falling in slow motion through space in free form fashion except always right side up. I seem to fall on something very soft e.g. stack of hay or feathers because the landing was not sudden but once again was in slow motion with my appendages floating freely. After it was over which in actual time was very short I felt fine I enjoyed the experience for it was nothing like I have ever experienced. I suffered no after effects the following day or thereafter.

Objective and Subjective Findings.—The mean values for number of items correct, number of trials, and percent scores for the Symbol Analogy, Digit Symbol and Addition tests are given in Tables 1, 2, and 3. Significant differences were found between pretest scores and the scores of tests administered during the high for the total group (n = 24) on the DS and

TABLE 2
MEAN NUMBER TRIED ON COGNITIVE TESTS

Subject AD Group	PreTest			High			5 minutes			10 minutes		
	SA	DS	AD	SA	DS	AD	SA	DS	AD	SA	DS	
	P	P	P	H	H	H	5	5	5	10	10	10
Male Straight (6)	8.33	44.5	8.00	11.5	35.7	6.50	11.2	45.5	8.00	10.8		
43.5	7.67											
Female Straight (6)	9.50	49.5	7.17	11.5	48.0	6.33	11.7	51.2	7.67	11.3		
50.8	8.17											
Total Straight (12)	8.92	47.0	7.58	11.5	41.8	6.42	11.4	48.3	6.92	7.67		
46.8	6.50											
Male Freak (6)	11.3	44.0	8.83	11.5	28.3	6.67	13.7	44.8	8.83	11.8		
45.8	9.00											
Female Freak (6)	13.0	46.2	7.67	13.2	40.7	5.83	14.7	46.3	7.33	13.8		
49.3	7.33											
Total Freak (12)	12.2	45.1	8.25	12.3	34.5	6.25	14.2	45.6	8.08	12.9		
47.6	8.17											
Total Subjects (24)	10.5	46.0	7.92	11.9	38.2	6.33	12.8	47.0	7.96	12.0		
47.4	8.04											

TABLE 2
MEAN PERCENT SCORES ON COGNITIVE TESTS

Subject Group	PreTest			High			5 minutes			10 minutes		
	SA	DS	AD	SA	DS	AD	SA	DS	AD	SA	DS	AD
	P	P	P	H	H	H	5	5	5	10	10	10

Male Straight (6)	72.3 99.7	100	82.0	56.0	97.7	75.2	64.0	99.7	90.2	64.6	
	78.1										
Female Straight (6)	88.3 82.7	100	97.9	76.2	99.3	88.7	74.1	100	87.0	76.6	98.8
Total Straight (12)	80.3 99.2	100	90.0	66.1	98.5	82.0	69.0	99.8	88.6	70.5	
	80.4										
Male Freak (6)	84.6 82.2	100	91.1	81.8	97.5	79.5	76.9	100	91.6	83.7	100
Female Freak (6)	81.5 100	100	88.6	77.5	99.1	83.6	75.2	100	91.3	84.7	
	90.8										
Total Freak (12)	83.1 86.5	100	89.8	79.6	98.3	81.5	76.0	100	91.4	84.2	100
Total Subjects (24)	81.7 83.4	100	89.9	72.8	98.4	81.7	72.5	99.9	90.0	77.4	99.6

AD, but not the SA ((please put symbol here)>.01; Tables 4+5). The significantly lower performance during the high was found not only on number correct, but on number varied and percent correct as well. There were no significant differences between pre-test and tests during the 5 and 10 minute periods.

The only other significant differences when groups (straight/freak or male/female) were compared were as follows:

1. Women did better than men on DS at the high: Number Correct – sig = .019; Number Tried - sig = .020.
2. Freaks did better than straights on the SA during the pre-test: Number Correct – sig = .040; Number Tried – sig = .035.
3. Freaks did better than straights on the SA at 5 minutes: Number Correct – sig = .030; Number Tried – sig = .040.

In Terms of adaptation phenomena there were no significant differences when the same test was compared at the high for all three trials.

There was a significant difference for SA at 10 minutes with improvement from trial 1 to trial 3.

TABLE 4
COMPARISON OF MEAN CORRECT SCORES
OF ALL SUBJECTS
(LEVELS OF SIGNIFICANCE)

	Tests		
	SA	DS	AD
Pre-High	.899	*.003	*.002
Pre-5 minutes	.410	.648	.929
Pre-10 Minutes	.487	.564	.438

TABLE 5
COMPARISON OF MEAN TRIALS
OF ALL SUBJECTS
(LEVELS OF SIGNIFICANCE)

	Tests		
	SA	DS	AD
Pre-High	.152	*.005	*.006
Pre-5 minutes	*.010	.634	.927
Pre-10 Minutes	.125	.498	.792

High-5 Minutes	.546	*.001	*.003		.322	*.002	*.008
High-10 Minutes	.633	*.001	*.018		.962	*.002	*.007
5-10 Minutes	.870	.908	.420		.303	.849	.872

There were several general findings regarding subjective experiences. All Ss reported a pleasant experience (calm, euphoria' relaxation, orgasm-like) which seemed to heighten or be prolonged in most cases with repeated exposure. The duration of the peak effects of N₂O were from 20 seconds to 3 minutes for both freaks and straights.

Nine straights and nine freaks experienced auditory sensations including ringing, buzzing, increased volume, dampening of volume, illusions and possible hallucinations. Visual effects were uncommon. One freak noted darkening of what he saw and three straights indicated blurring of vision, visual pulsing or increased brightness. Ten straights and 7 freaks reported numbness and/or tingling — usually about the mouth or in the extremities. Eight straights described warm feelings (around the head or total body) while only 3 freaks had this experience. Sensations of light-headedness, dizziness, floating or motion were reported by 8 straights and only one freak.

Most of the straights likened the experience to the effects of alcohol or sexual orgasm. The freaks compared it to psychedelic drugs, feeling it was a more immediate, higher high but of shorter duration. Both groups felt poorly motivated during the high. Many felt the tests were silly and generally did not want to be bothered by external demands.

Adverse experiences were minimal. Seven straights described various states they felt unpleasurable—light nausea the first time a reminder of a previous uncomfortable experience; a bloated sensation; a pulsating pressure; decreased sense of control; warmth; dry throat. Only one freak described a dysphoric state—one of mild suspiciousness.

Depersonalization-like experiences were noted by 2 straights and one freak.

Residual effects lasting from second's (straight) to 14 hours (freak) included decreased concentration, relaxation, tingling, light headedness, giddiness, mellowness, warmth and increased sensory awareness.

Several subjects (4 straight and 3 freak) reported a lessening of dysphoric sensations, which were present before inhalation (anxiety, tension, boredom and fatigue). Eleven of the freaks were willing to engage in further research with nitrous oxide. The twelfth wanted further experiences but not under experimental conditions. Two of the straights (husband and wife) indicated that they would not choose to participate in further work. The man had a "flashback" of a previous uncomfortable situation which he either could not or was unwilling to describe.

DISCUSSION

It would appear that the non-medical use of nitrous oxide is on the increase in mid-Michigan. In the manner that the drug is generally used (breathholding of pure nitrous oxide from a balloon or rebreathing) it appears to be a safe procedure. The acute onset of effects (15-30 seconds) is likely related to the rapid pick up of the gas by the blood in the lungs and one circulation time to the brain. Cognitive functioning is diminished during the peak of the high at least when measured by DS and AD testing but returns to normal within five minutes. There seems to be little difference in effects on cognitive functioning when freaks are compared with straights. The deficiencies in cognitive abilities may be related both to delirium and decreased motivation. Based on the three trial method employed there seems to be no adaptation to the cognitive deficits provoked by the nitrous experience.

Subjective responses are similar for both groups with some differences in physical sensations. Freaks seem to have after effects for longer periods of time, which may be more, related to previous experiences, personality and expectations than to the effect of the drug. The possibility exists of 'reverse tolerance'—that either less of the drug is required for the same effect with subsequent trials or the same dosage leads to greater effects.

Nitrous oxide is not without danger. Its delirigenic effects will undoubtedly impair performance. In addition there have been reports in the press and anecdotally of individuals who suffocated by using N₂O in a closed system (e.g. closed automobile, tightly fitting mask).

Some of our findings will be pursued in the near future. The tranquilizing effects of the agent will be tested in behavioral modification treatment; in addition we would like to explore the possibilities of the effects of N₂O on individuals who are addicted to alcohol or opiates.

SUMMARY

A survey of the prevalence of the non-medical use of N₂O made in mid-Michigan suggests an increase in usage. A total of 34 volunteer's self-administered pure nitrous oxide from balloons. Subjective findings generally indicated pleasurable effects, which were, in the main, similar for freaks and straights. Cognitive defects were noted during the peak high but returned to normal within 5 minutes.

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