

# On the Potential Utility of Nitrous Oxide in Psychedelic Psychotherapy: A Pilot Study

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## INTRODUCTION

Nitrous oxide ( $N_2O$ ) is a colorless gas with a slightly sweet odor that is commonly used as an analgesic in dentistry. Its safety and efficacy in this application has been well established. Effects of  $N_2O$  on personality have been described by Biersner, Edwards & Bailey (1974) as including less environmental attention, increased interpersonal responsiveness and withdrawal. Lynn et al. (1972) have reviewed the history of the use of  $N_2O$  in applications other than dentistry, including self-administration for recreational purposes. Recreational use seems to be increasing rapidly within the current drug subculture. These authors also report the results of the administration of  $N_2O$  to 34 volunteers, concluding that performance on cognitive tasks is impaired and that the subjective experiences are almost uniformly reported to be pleasant. Subjects without previous experience with psychedelic drugs "likened the experience to the effects of alcohol or sexual orgasm," while those with a history of drug use compared the subjective response to that engendered by psychedelics, "feeling it was a more immediate, higher high but of shorter duration." The reported similarity of the effects of  $N_2O$  to the effects of psychedelics raises the possibility that  $N_2O$  could be used as an adjunct to psychotherapy in the same way that other psychedelics have been (Grof 1975; Pahnke et al. 1971). The fact that the effects of  $N_2O$  dissipate quite rapidly would make it a particularly promising agent, if it were found to

produce significant psychedelic effects, since this quality of its action would allow its convenient use on an outpatient basis. The present study was therefore undertaken with the intent of determining the extent to which  $N_2O$  produces effects that are similar to those produced by psychedelic compounds such as LSD and might therefore be expected to be useful in the context of psychedelic psychotherapy.

## METHOD

It appears that a salient quality of psychedelic compounds that makes them of unique value in psychotherapy is their ability to evoke, under proper circumstances, a "peak experience" or "psychedelic reaction." Such a subjective response has been quantitatively defined by Pahnke (1969) in terms of the categories of experience usually associated with spontaneous mystical experiences, and these categories have in turn been incorporated at the Maryland Psychiatric Research Center into an instrument entitled the Psychedelic Experience Questionnaire (PEQ). This instrument provides scores on seven subscales (Internal Unity, External Unity, Sense of Sacredness, Objectivity and Reality, Transcendence of Time and Space, Deeply-Felt Positive Mood and Ineffability) as well as a total score. The Ludwig-Levine modification of the Linton-Langs Questionnaire (LLQ) is another instrument that has been used to quantify the subjective responses to LSD when this compound is used as an adjunct to psychotherapy (Ludwig, Levine & Stark 1970). Although not intended to measure as unitary a response

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as the peak experience is presumed to be, it nevertheless gives a total score and scores on eight subscales (Alteration in Thinking, Disturbed Time Sense, Loss of Control, Meaning Change, Affect Change, Body Image Change, Somatic Change and Perceptual Change). It was therefore decided to administer the PEQ and the LLQ to a sample of persons recently exposed to N<sub>2</sub>O in order to determine to what extent a psychedelic type of reaction was engendered.

In the interests of economy a population was sought that was going to be exposed to N<sub>2</sub>O for purposes other than the present experiment. Those using the drug informally for recreation were considered but rejected because of possible legal difficulties, complications of recruitment and inability to accurately assess dosage. Since it was necessary to study subjects who were given sub-anesthetic doses, in order that they might be conscious during the intoxication and hence able to recount their experiences, a population of dental patients was chosen. Three local dentists who use N<sub>2</sub>O in their practices were approached and agreed to participate. They were asked to solicit participation in the study from patients to whom they administered N<sub>2</sub>O. Patients who agreed to participate were given a packet containing the PEQ, LLQ, a questionnaire requesting additional background information about the patient, a cover letter containing instructions and an explanation of the research project and a stamped and addressed envelope in which to return the questionnaire to the author. The dentist also completed a form describing the exposure to N<sub>2</sub>O in terms of the amount of oxygen (O<sub>2</sub>) mixed with it (in dental work N<sub>2</sub>O is usually mixed with an approximately equal volume of O<sub>2</sub>), the degree to which this mixture was diluted by allowing room air to be breathed by the patient simultaneously and the duration of the exposure.

### Subjects

A total of 20 subjects, 10 males and 10 females, completed and returned the questionnaires. The females ranged in age from 28 to 55 ( $M = 40.2$ ) and the males ranged from 26 to 61 ( $M = 39.5$ ). All subjects were judged by their dentists to be free from obvious psychopathology, and the sample therefore is presumed to consist of normal volunteers.

### RESULTS

Means and standard deviations for each of the scales of the PEQ and the LLQ are presented separately for males, females and the entire sample in Table 1. The final column reveals that all of the scores are significantly different from zero for the entire sample.

The same is true for the scores of the males and females taken separately on the LLQ. On the PEQ, however, there were three scales that did not achieve such statistical significance for the sexes separately: External Unity for the males, and Internal Unity and Sense of Sacredness for the females.

The subscales of the PEQ tended to intercorrelate positively among themselves and each showed a significant positive correlation ( $p < .001$ ) with the total score on this instrument. A similar but weaker pattern of intercorrelations was observed among the subscales of the LLQ, and the correlations of the subscales with the total score, though positive in all cases, only reached significance ( $p < .05$ ) for five of the eight subscales. Nevertheless it was felt that there was sufficient internal consistency within both instruments to justify using only the total score from each in order to explore possible dose/response relationships.

Dosage was quantified in seven separate ways. This was made possible by the fact that the procedure for using N<sub>2</sub>O in dental work involved first mixing it with oxygen and then allowing the patient to breathe the N<sub>2</sub>O/O<sub>2</sub> mixture through a mask, which in turn has an adjustable valve to permit a certain amount of room air to mix with the N<sub>2</sub>O/O<sub>2</sub> mixture as it is inhaled. This procedure allowed for the derivation of the following seven parameters of dose: N<sub>2</sub>O/O<sub>2</sub> mixture flow rate (liters per minute), N<sub>2</sub>O/O<sub>2</sub> mixture ratio (liters per minute N<sub>2</sub>O divided by liters per minute O<sub>2</sub>), total mixture concentration (liters per minute N<sub>2</sub>O/O<sub>2</sub> mixture divided by liters per minute of total volume inhaled, including room air), exposure time (minutes), percent N<sub>2</sub>O in total mixture (liters per minute N<sub>2</sub>O divided by liters per minute total mixture), N<sub>2</sub>O flow rate (liters per minute), total N<sub>2</sub>O (liters). None of these showed significant correlations with either PEQ total or LLQ total.

Sex differences were minimal. No significant differences were found between males and females on any of the individual variables measured in the study (including descriptive characteristics such as age from the background questionnaire, parameters of dosage and all scales of the PEQ and LLQ). However, across the seven subscales of the PEQ there was a tendency for the males to score higher. When the mean scores for the males on these seven scales are compared with the means for the females, the difference is almost significant ( $t = 2.21$ ,  $p = .06$ ). There were a few minor differences between the sexes in the patterns of intercorrelations between variables, the most remarkable of which was in the correlations between N<sub>2</sub>O/O<sub>2</sub> mixture flow rate and the Disturbed Time Sense scale of the LLQ. The

TABLE 1  
MEAN SCORES ON PEQ AND LLQ

Scale	Number of Items	Males (N = 10)		Females (N = 10)		Entire Sample (N = 20)	
		mean	s.d.	mean	s.d.	mean	s.d.
<b>PEQ</b>							
Internal Unity	30	2.7*	4.5	1.7	3.2	2.2**	3.8
External Unity	30	3.1	5.7	2.4*	3.9	2.8**	4.8
Sense of Sacredness	35	3.7*	5.1	2.8	5.9	3.3**	5.4
Objectivity and Reality	20	3.3*	4.4	2.6*	3.9	3.0†	4.0
Transcendence of Time and Space	40	5.8*	8.1	5.5†	5.3	5.7†	6.7
Deeply Felt Positive Mood	35	10.0†	6.6	5.8*	6.7	7.9††	6.7
Ineffability	25	5.3†	4.3	5.1*	6.2	5.2††	5.1
TOTAL	185 <sup>a</sup>	31.9†	26.1	24.3*	27.3	28.1††	26.3
<b>LLQ</b>							
Alteration in Thinking	13	2.3**	2.4	3.3†	2.3	2.8††	2.4
Disturbed Time Sense	5	1.1†	0.9	1.8†	1.7	1.5††	1.4
Loss of Control	15	2.8**	2.9	3.6†	3.2	3.2††	3.0
Meaning of Change	11	2.0*	2.5	1.5	2.6	1.8†	2.5
Affect Change	6	1.8†	1.5	1.2†	1.0	1.5††	1.3
Body Image Change	12	1.8††	1.1	2.3††	1.5	2.1††	1.3
Somatic Change	11	1.5†	1.3	1.5†	1.4	2.0††	1.4
Perceptual Change	16	1.5*	1.8	1.1*	1.3	1.3†	1.6
TOTAL	89	14.6†	10.1	16.4††	8.7	15.5††	9.1

\* Significantly different from 0 at the .05 level.

\*\* Significantly different from 0 at the .01 level.

† Significantly different from 0 at the .005 level.

†† Significantly different from 0 at the .0005 level.

<sup>a</sup>In computing the total score only one of the first two scales (Internal Unity and External Unity) is used, whichever is higher.

correlation between these two variables was  $r = .79$  ( $n = 10$ ,  $p = .007$ ) for females and  $r = -.18$  ( $n = 10$ ,  $p = .611$ ) for males. Across the subscales of the PEQ and the LLQ males and females showed similar profiles. The correlations between the means on the subscales for the two sexes were  $r = .86$  ( $n = 7$ ,  $p < .02$ ) on the PEQ and  $r = .77$  ( $n = 8$ ,  $p < .05$ ) on the LLQ.

#### DISCUSSION

The data from the present study indicate that scores on the LLQ and PEQ tend to be significantly elevated

above their presumed baseline of zero by the administration of  $N_2O$  in a dental setting. Although this finding offers some promise for using  $N_2O$  as an adjunct to psychotherapy within a psychedelic model, the study suffers from a number of shortcomings that moderate the significance of the findings.

One shortcoming is the absence in the existing literature of clear normative data for the PEQ and the LLQ. Inspection of the items contained in the scales (e.g., PEQ item 14: experience of oneness or unity with objects and/or persons perceived in your surroundings)

indicates that they are non-trivial and unlikely to be endorsed by a subject in normal waking consciousness, a fact that lends potential psychotherapeutic significance to the statistical significance of the differences of the mean scale scores from zero. However, the rather low absolute values of these means must be noted. Normative data of a sort is available in a report by Richards et al. (1977) in which it was found that cancer patients treated for anxiety and depression with a known psychedelic (dipropyltryptamine) could be divided into those who produced high versus low scores on the PEQ in response to that treatment. The high scorers were defined as having a total PEQ score of 111 or higher, as contrasted with the mean for the present sample of nitrous oxide patients of 28.1. Whether N<sub>2</sub>O employed in a psychotherapeutic framework and/or higher dosage would produce comparable results remains an open question. Clearly the set and setting would be different if one were using N<sub>2</sub>O as an adjunct to psychotherapy, as opposed to using it as a dental analgesic.

The basic correlational design of the present study is cause for further ambiguity, and accordingly caution, in interpreting its results. In addition to the general limitations of such a design, it should be noted that the dentists involved determined dosage of N<sub>2</sub>O not only on the basis of physical variables such as body weight and type of dental work to be performed, but that in some cases they also attempted to compensate for what they estimated to be the patient's psychological resistance to the drug. Hence no pretense can be made that a standard dosage was administered.

Although the dosage was not standardized, the range of doses given was apparently not great enough to allow any significant dose/response relationships to emerge. Harris (1973), on the other hand, also failed to find differences in response when he deliberately manipulated dosage in a systematic way. It may be the case that the response to N<sub>2</sub>O, when administered at a dose level that is above the threshold for psychological effects, but sub-anesthetic, tends to be a rather all-or-none affair. If this is the case, then any significant enhancement of its effects for psychotherapeutic purposes would have to be achieved by changes in set and setting, rather than dosage.

One rather interesting correlation that emerged from the data is almost impossible to interpret because of the correlational design of the study. A number of the subscales of the PEQ and of the LLQ showed significant negative correlations with Exposure Time and with total N<sub>2</sub>O (the latter two variables were significantly positively correlated, as would logically be expected,

with  $r = .85$ ,  $n = 20$ ,  $p < .001$ ). This apparent decrement in the intensity of the subjective effects when exposure is prolonged (and consequently there is an increase in the total amount of N<sub>2</sub>O inhaled) can be interpreted in at least two ways. It may be an artifact of the setting, whereby longer exposures were associated with more major, and perhaps more painful, dental procedures. Or N<sub>2</sub>O may possess some unique property such that subjective effects are maximized by relatively acute administration. Such a property would certainly have a bearing on the format in which the compound might be employed as an adjunct to psychotherapy.

Earlier studies have indicated the potential utility of N<sub>2</sub>O as an adjunct to both analytically oriented (Rogerson 1944) and behaviorally oriented (Harris 1973) forms of therapy. In addition, recall that the subjects of Lynn et al. (1972) who had previous experience with psychedelics likened the effects of N<sub>2</sub>O to psychedelic drugs (while those without such experience compared the effects to alcohol and sexual orgasm). Finally, it is noted that almost all previous work has indicated the apparent safety of N<sub>2</sub>O when used in sub-anesthetic dosage, with the single exception to this rule (Brodsky & Zuniga 1975) being based on multiple daily administrations over a six-month period. Taken together with the results of the present study, these data argue strongly for some experimental exploration of the potential of N<sub>2</sub>O within a psychedelic psychotherapy framework. Given the relative lack of restrictions on the use of N<sub>2</sub>O at the present time, such explorations should be well within the range of possibilities for many researchers interested in this field.

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