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Title: TIME COURSE OF MENTAL EFFECTS OF 30% NITROUS OXIDE DURING INHALATION AND RECOVERY

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**Introduction.** Subanesthetic concentrations of N<sub>2</sub>O are widely used for analgesia and are occasionally abused. The kinetics of uptake and elimination of N<sub>2</sub>O have been adequately studied,<sup>1</sup> but pharmacokinetics cannot directly answer the question; how soon and for how long do mental and psychomotor functions become impaired during and after administration of N<sub>2</sub>O. It, therefore, seemed important to study the time course of mental and psychomotor effects of N<sub>2</sub>O during inhalation and recovery.

**Methods.** Twenty-two young healthy volunteers participated in the trial. Each subject signed an informed consent form and the study protocol was approved by the Univ. of Iowa Committee on Research Involving Human Subjects. After a practice session, 11 subjects inhaled 30% N<sub>2</sub>O, and 11 inhaled O<sub>2</sub> only. The concentration of N<sub>2</sub>O in end-tidal air was continuously measured using an infrared analyzer (Beckman LB-II). The subjects' mental and psychomotor skills were measured before the gas administration and 2, 12, 22 and 32 min after establishing the 30% end-tidal air concentration of N<sub>2</sub>O using a free recall, tapping board and arithmetic tests. Subjects then breathed room air and the tests were repeated 2, 12, 22 and 32 min after discontinuation of the gas (first recovery phase). After an interval of 30 min, the subjects were challenged a second time with the same gas. The above tests were again administered at 12 and 32 min during the inhalation and free recall was again measured at 32 min after discontinuation of the gas (second recovery period). The subjects also rated their feelings on visual analogue scales and they were asked at the end of the experiment whether they thought they had received O<sub>2</sub> alone or N<sub>2</sub>O. A multivariate analysis of variance was used for statistical treatment of the results.

**Results.** Six and 8 out of the 11 subjects who received O<sub>2</sub> and N<sub>2</sub>O, respectively, thought they received N<sub>2</sub>O. Both administrations of N<sub>2</sub>O induced significant (P<0.005-P<0.001) mental and physical sedation when compared to baseline or O<sub>2</sub> administration. The latter did not modify the subjects' performance in any of the tests used. When compared to baseline or O<sub>2</sub> administration, N<sub>2</sub>O decreased (P<0.005-P<0.001) the number of words recalled in the free recall test (Fig. 1). The maximum effect was already present at the 2-minute testing period and remained unaltered throughout the rest of the inhalation. The number of words recalled had returned to baseline 12 minutes

after discontinuation of N<sub>2</sub>O. No differences were found between the effects of the first and second administration of N<sub>2</sub>O and recovery was similar after both administrations. The results in tapping board and arithmetic tests were similar to those shown in Fig. 1 for the free recall test, i.e. the performance was already impaired at the 2-minute testing period and stayed similar throughout the rest of the N<sub>2</sub>O inhalation and the second administration results were similar to the first, as was the second recovery phase. The recovery of tapping rate, however, was slower than that of free recall. Tapping rate was still impaired at 12 min but had returned to baseline at 22 min after discontinuation of N<sub>2</sub>O.

**Discussion.** The kinetics of mental and psychomotor effects of N<sub>2</sub>O paralleled the kinetics of its uptake and distribution.<sup>1</sup> In mice acute tolerance to loss of righting reflex developed during the first 10 min of exposure to N<sub>2</sub>O.<sup>2</sup> Our results do not show development of tolerance to mental and psychomotor effects. Recovery was complete in 22 min and repeated administration produced similar results to the first administration as did the second recovery phase.

#### References.

1. Eger EI, Anesthetic Uptake and Action. Baltimore, Williams and Wilkins, 1974, pp 77-96, 228-248.
2. Smith RA et al: Anesthesiology 50:496-500, 1979.

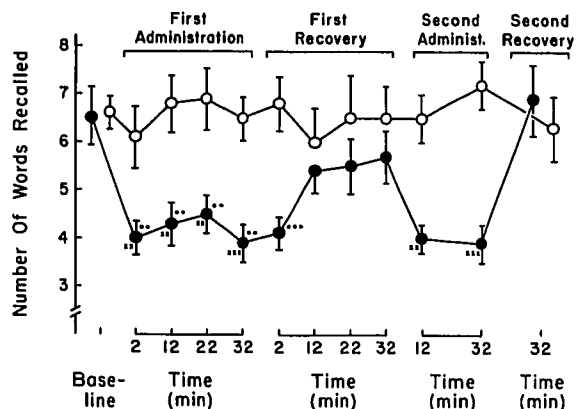


Fig. 1. The number of words recalled in free recall test before, during and after repeated administration of 30% N<sub>2</sub>O (●) or oxygen (○). \*\* = P<0.005, \*\*\* = P<0.001 vs. baseline and xxx = P<0.001 vs. oxygen.