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Opinion

Opioid Activity of Nitrous Oxide and Ketamine

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I read the excellent recent paper by Eslaamisaad and Topic [1] with interest. Nonetheless, some of their statements need modification. For instance, they state "Recent studies have suggested that both N – methyl – D - aspartate (NMDA) and Gamma - aminobutyric acid type A (GABA - A) receptors are affected by nitrous oxide" and later in the paper "Ketamine generates its effects through an antagonistic action on NMDA receptors…." Unfortunately, there is no mention of the opioid system in the actions of either nitrous oxide or ketamine.

There is good and abundant evidence clearly showing that the endogenous opioid substances and receptors are involved in the actions of both nitrous oxide (N_2O) and ketamine.

First, let us look at the evidence for endogenous opioid participation in the actions of nitrous oxide (N_2O). Readers will note that these studies have been conducted in both animals and man, conclusively showing that N_2O has opioid properties [2,3]. Some of these publications indirectly implicate the endogenous opioid system in the actions of N_2O [4-11]. There are also radio - receptor binding studies that indicate that N_2O acts directly on opioid receptors, in animals [12,13] and man [14]. It is also of interest that N_2O, and not nitric oxide (NO), was the first gas to have been showed to have a role in neurotransmission [15,16]. It is also clear from some these studies that N_2O is a partial opioid agonist [2,3].

Second there is also good evidence, that ketamine interacts with endogenous opioid system [8,17-20]. Although more research needs to be done to establish whether it does so by binding directly to opioid receptors (like N_2O) or merely by provoking the release of endogenous opioids.

Of course, they are quite correct in averring that N_2O interacts with other receptor systems apart from the opioid system [1].

These authors [1] also mention that "The dose of nitrous oxide is 50% combined with 50% oxygen in the mixture". There are good reasons to take issue with the routine use of a 50:50% mixture of nitrous oxide and oxygen. Rather the required concentration of N_2O should be titrated to the individual requirements of each patient, by employing the gentler dental titration technique, to avoid unnecessary side effects. The side effects associated with a fixed 50% mixture of N_2O and oxygen include, nausea, vomiting, pre - anaesthetic excitation or even actual anaesthesia [20-22].

I think it is important to bring this information to the attention of your readers.

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Nil.

Conflict of Interest

I have been researching and publishing on the psychotropic properties of nitrous oxide for over 40 years. Since 2003, I have been a medical adviser to Sedatek, a South African company that supplies equipment for administering low concentrations of nitrous oxide in South Africa, predominantly among dentists. I own no shares in the company.

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