

Rising Nitrous Oxide Use & Clinical Implications for CL Psychiatrists: A Case Series

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INTRODUCTION

Nitrous oxide (N₂O) is an odorless, colorless gas used in medicine for its anesthetic effects since 1844. Known also as “laughing gas” it is misused recreationally because of its rapid euphoric and dissociating effects.

Nitrous oxide is commonly misused among young adults and its lack of regulation make it easily available.

Nitrous oxide inactivates cobalamin and its chronic misuse can lead to variety of neuropsychiatric symptoms due to functional vitamin B12 deficiency (Figure 1 & 2).

We present three patients admitted to the hospital with N₂O misuse to describe the demographics, spectrum of neuropsychiatric presentations, and treatment strategies for consultation-liaison (CL) psychiatrists.

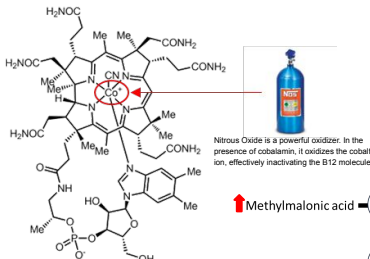


Figure 1. Site of cobalamin inactivation by nitrous oxide

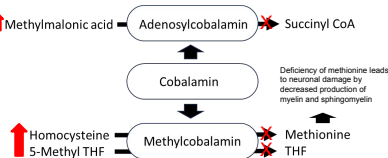


Figure 2. Metabolic effects of cobalamin inactivation

CASES

Case 1: A 24 year old Chinese female with nitrous oxide use disorder was admitted to the hospital for proprioceptive ataxia. She presented with disorientation, inattention, auditory and visual hallucinations, and paranoia. She received vitamin B12 1000 mcg daily and an antipsychotic with resolution of her psychosis.

Case 2: A 22 year old Chinese female with nitrous oxide use disorder and ketamine use disorder was admitted to the ICU for severe hyponatremia as a complication of ketamine use disorder. She showed psychiatric symptoms of irritability, low mood, and emotional lability. She did not show significant complications from nitrous oxide use. She left as a patient-initiated discharge two days after admission.

Case 3: A 23 year old Chinese female with inhalant use disorder was admitted to the physical rehabilitation service for subacute combined spinal degeneration after presenting with urinary retention and paraparesis. She initially was started on intramuscular vitamin B12 1000 mcg weekly and intensive PT and OT. After being seen by psychiatry, she was started on oral vitamin B12 1000 mcg daily. She was discharged after 3 weeks of intensive PT and OT.

Table 1. Neuropsychiatric sequelae of nitrous oxide misuse

Neurologic	Psychiatric
<ul style="list-style-type: none"> Numbness Paresthesias Weakness Impaired gait Impaired coordination Cognitive impairment Bowel and bladder dysfunction Sexual dysfunction Hermite's sign 	<ul style="list-style-type: none"> Delusions (paranoia) Hallucinations (auditory, visual) Delirium Depression Anxiety/Panic Irritability Grandiosity Mania Suicidality

DISCUSSION

Our case series describes three young Chinese females with nitrous oxide use disorder. Nitrous oxide misuse is a growing concern amongst young adults, including Chinese youth (Chen et al., 2018).

Nitrous oxide can cause severe and varied neuropsychiatric symptoms through the inactivation of vitamin B12, as seen in our case series (Table 1) (Garakani et al., 2018).

While there is limited evidence for treatment, current literature suggests abstinence from nitrous oxide and short-term daily supplementation of vitamin B12 1000 mcg (Sluys et al., 2022). Our CL psychiatry team recommended a treatment strategy of daily supplementation of vitamin B12 1000 mcg indefinitely until neuropsychiatric symptoms resolve.

An antipsychotic and/or mood stabilizer may be necessary for co-occurring psychiatric symptoms, although there are no pharmacologic treatments for relapse prevention. Our three cases underscore the need for further research into demographic and structural factors that may be contributing to rising nitrous oxide misuse in young adults.

CONCLUSIONS

Nitrous misuse can lead to significant neuropsychiatric morbidity. CL psychiatrists should be aware of the growing rise in use and be able to identify neuropsychiatric symptoms of misuse, along with treatment interventions.

REFERENCES

- Chen R, Liao M, Ou J. Laughing gas inhalation in Chinese youth: a public health issue. *Lancet Public Health*. 2018 Oct;3(10):e465.
- Garakani A, Jaffe RJ, Savila D, Welch AK, Protin CA, Bryson EO, McDowell DM. Neurologic, psychiatric, and other medical manifestations of nitrous oxide abuse: A systematic review of the case literature. *Am J Addict*. 2018 Aug;25(5):358-69.
- Sluys Y, Vanherpe P, Amir R, Vanhoenacker F, Vermeersch P. Vitamin B12 deficiency in the setting of nitrous oxide abuse: diagnostic challenges and treatment options in patients presenting with subacute neurological complications. *Acta Clin Belg*. 2022 Dec;77(6):955-961.