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Mini Review

Opioid-Induced Nodding-Not a Nice Nap

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Abstract

Opioid-induced "nodding" is commonly misinterpreted as benign sleep but represents a high-risk state of fluctuating consciousness caused by drug-induced respiratory depression. This condition may lead to progressive hypoxia and hypercapnia without normal protective arousal. In the fentanyl era, nodding may reflect a subclinical overdose, with a dangerously narrow transition between sedation and fatal respiratory failure, particularly when opioids are combined with alcohol, benzodiazepines, or other sedative agents. We utilized PUBMED to adopt various works linked to this important topic. Accumulating clinical and neuroimaging evidence suggests that repeated non-fatal overdose events and nodding episodes may contribute to cumulative hypoxic–ischemic brain injury, hippocampal volume loss, and persistent cognitive impairment. Current surveillance systems largely emphasize mortality, thereby underestimating the neurological burden among survivors. Public health and clinical frameworks should redefine nodding as a sentinel respiratory-compromise state and prioritize early intervention, expanded reporting, and improved harm-reduction strategies.

Keywords: Nodding; Sleep; Opioid Use Disorder (OUD)

Key Points

- Experts estimate non-fatal drug overdoses affect at least a million people per year in the U.S.
- "On the nod" or "nodding" is a dangerous opioid state when the person drifts in and out of consciousness.
- Hypoxia causing memory impairment and behavior changes can follow overdoses, near overdoses, and nodding off.

Introduction

Many people who misuse opioids experience "nodding," a symptom of severe drowsiness resembling a person falling into a deep sleep but actually reflects a semiconscious state following drug use (commonly opioids like heroin or fentanyl) [1]. Nodding off is a dangerous, often involuntary condition characterized by the head nodding forward while the person drifts between consciousness and sleep. Nodding may indicate a severe oxygen deprivation and an excess of carbon dioxide accumulation preceding an overdose [2]. Recent brain imaging data suggest that nodding may contribute to damage in oxygen-sensitive brain areas [3]. It's important to know that opioid-overdose-related brain injuries resemble global hypoxic-ischemic brain injury, the same injury class seen after near-drowning, choking/asphyxiation, or cardiac arrest. All are primarily oxygen deprivation injuries [4-7].

Drug overdose deaths have dropped significantly but remain unacceptably high [8]. Interruptions in the drug supply chain and increased availability of naloxone for reversing overdoses have been major contributors to this progress [9-11]. But for every fatal drug overdose, there are many more often ignored, non-fatal overdoses, and their immediate as well as cumulative effects are very dangerous [12]. Opioid misuse and addiction, with or without overdoses, damage key brain regions involved in memory [13]. "On the nod" often represents subclinical overdose, and repeated episodes may contribute to cognitive impairment, neurocognitive consequences of repeated opioid-related hypoxia, cardiac arrhythmias, and hypoxic brain injury, especially with fentanyl [14]. We know many overdoses aren't reported, whether the rescued person overdosed at home or elsewhere, and took naloxone. In 2023, U.S. pharmacies dispensed more than 2.1 million naloxone prescriptions, a significant increase from earlier years (1.7 million in 2022) [15]. According to Casillas., *et al*. from 2010 through 2020, there was approximately one fatal overdose for every 15 non-fatal overdose. Thus, if roughly 80,000 people died annually from overdoses, total overdoses (fatal + non-fatal) likely exceeded one million annually [16].

NOT a Nice Nap

An individual experiencing opioid-induced nodding may appear deeply asleep: the head droops forward, eyes close halfway, speech slows or trails off, and the body becomes slack and heavy. A person may briefly respond to verbal or tactile stimulation, fading into silence moments later. Someone who arouses briefly but immediately nods off is not "safe." Emergency medicine providers don't and shouldn't trust patients saying they're "fine," or receiving information like, "He always nods like this," or "She's just high." This is not normal sleep. Many describe it as a sensation of floating or slipping between wakefulness and rest. Nodding is often sought rather than perceived as the dangerous warning sign it is. Opioids depress brain regions responsible for alertness and breathing. They also reduce brain responsiveness to carbon dioxide, which normally stimulates breathing and helps maintain wakefulness. As opioid levels rise, breathing becomes shallower, carbon dioxide levels increase, and sedation deepens. The person may appear fine; however, the body is under impaired respiratory control [17].

New studies show opioid use disorder (OUD) is associated with reduced cerebral oxygen availability, damaging brain cells, suggesting users cannot tell they've had an overdose [18]. Repeated opioid nodding episodes may produce persistent neurobiological changes by interrupting oxygen delivery, rather than direct neurotoxicity's. OUD itself is associated with smaller hippocampal volumes (replicated across multiple samples) [19]. There is credible evidence that an overdose can be a brain-injury event, even when "reversed," and patients appear neurologically intact [20].

A nodding person on opioids may be arousable to voice or light touch, breathing slowly but steadily. As opioid effects deepen, the same individual may become difficult or impossible to awaken, breathing may slow further or become irregular, and blood oxygen levels may fall. From the outside, these changes appear subtle. However, such individuals require urgent medical evaluation and intervention. A common misconception is that as long as a person still breathes, they are safe. This is not true. Opioid-induced breathing may be inadequate even when not stopping completely. Shallow or infrequent breaths can allow oxygen levels to drop without dramatic signs of distress. As oxygen falls and carbon dioxide rises, sedation deepens, creating a feedback loop leading to respiratory failure. Snoring, choking, or gurgling sounds, often mistaken for deep sleep, may indicate partial airway obstruction and worsening risk.

People using opioids may become accustomed to heavy sedation and feel safe because they "nodded" before without apparent harm. However, tolerance to the pleasurable/sedating effects of opioids may increase faster than the body's tolerance to respiratory depression. This imbalance is especially pronounced with drugs like fentanyl as well as opioids combined with alcohol, benzodiazepines, xylazine, and/or medetomidine or other sedatives. As a result, a dose familiar to users can dangerously suppress breathing [21].

Fentanyl and its analogs cause rapid, profound respiratory suppression and shallow breathing, and the margin between nodding and death is much narrower than in the heroin era. Fentanyl is often adulterated, containing xylazine or medetomidine. This makes hypoxia more likely. Medetomidine is significantly more potent than xylazine (100 to 300 times more) leading to deeper, longer-lasting sedation and hypoxia risks [23]. There is no safe intoxicated state once breathing is compromised.

Sedation impairing ventilation is an overdose. In the operating room, anesthesiologists use opioids to blunt pain and suppress reflexes under controlled conditions. Surgical patients often receive oxygen supplementation and continuous monitoring. The anesthesiologist intervenes immediately if oxygen saturation or breathing drops by stimulating, ventilating, or reversing opioids.

In contrast, when opioids are taken outside medical settings, the main danger is respiratory depression. Opioids blunt brainstem responsiveness to increased carbon dioxide and low oxygen. By the time a user realizes they are in distress, they may be unable to act. If prolonged, brain injury or death may occur. Opioid-induced respiratory depression causes breathing to become slow, shallow, and irregular, but these signs may be mistaken for falling asleep or snoring. Hypoxia can cause brain damage within minutes, even while the heart still beats.

A user, alone or with peers, almost never has an anesthesiologist's expertise, pulse oximeters, bag-mask ventilation capability, or naloxone to reverse a falling oxygen level. Pulse oximeters are inexpensive and easily purchased, but they are not part of the "drug use culture".

Wearable monitors combined with automatic alerts (such as smartwatches detecting hypoxia or a respiratory pause) could become harm-reduction tools and work in this area is emerging. But it might not help with potent synthetic opioids (fentanyl and adulterants) because respiratory depression can become profound in under a minute, faster than a person can read or react to a monitor.

Policy statement

Opioid-induced "nodding" should be addressed in public messaging, clinical guidance, and surveillance systems as a sentinel respiratory-compromise state, not a benign intoxication or ordinary sleep. It is important to distinguish this phenomenon from normal fatigue-related drowsiness. In physiological sleep onset, ventilatory drive and carbon dioxide responsiveness remain intact. By contrast, opioid-induced nodding reflects pharmacologic suppression of brainstem respiratory control, where oxygen levels may fall without the usual corrective arousal response.

Not every episode of opioid-related sedation results in clinically significant hypoxia, however, the absence of immediate collapse does not exclude impaired ventilation or cumulative physiologic risk, particularly in the context of high-potency synthetic opioids and poly-sedative exposure.

The United States has made measurable progress in reducing fatal overdoses, yet non-fatal overdoses and near overdoses remain widespread and frequently unreported. For every fatal overdose, many more individuals experience hypoxic events that do not enter mortality statistics. Current policy frameworks focus primarily on death counts, while cumulative hypoxic exposure and potential neurocognitive consequences among survivors remain largely unmeasured [See Table 1].

Rationale

In fentanyl-era drug markets, the margin between sedation and life-threatening respiratory compromise has narrowed considerably. Repeated hypoxic episodes, whether fatal or non-fatal, may plausibly contribute to cumulative neurologic vulnerability. An effective overdose strategy should therefore be evaluated not only by reductions in mortality, but also by its capacity to mitigate preventable brain injury and long-term disability among survivors.

Policy Implications
1. Clarify public health guidance. Public education materials should explicitly describe opioid-related nodding as a potential indicator of impaired ventilation. Sedation accompanied by slowed, shallow, or irregular breathing warrants emergency assessment, even if the individual appears arousable. 2. Expand surveillance beyond mortality metrics. Standardized reporting pathways should incorporate naloxone administrations, EMS non-transport encounters, emergency department reversals, and community-based interventions. Measuring fatal events alone underestimates the neurologic burden of opioid-related hypoxia. 3. Develop a post-overdose brain health pathway. Following overdose or near-overdose events, brief screening for cognitive or behavioral changes may be appropriate. Reversal of respiratory depression does not necessarily imply absence of transient or cumulative neurologic impact. 4. Strengthen harm-reduction tools with respiratory focus. Naloxone distribution remains essential. Training should emphasize airway positioning and ventilation support. Pilot programs evaluating low-cost pulse oximetry or wearable alert systems may provide additional data, recognizing limitations in the context of rapidly acting synthetic opioids. 5. Address poly-sedative exposure explicitly. Public health messaging and clinical practice guidelines should emphasize the heightened respiratory risk associated with opioids combined with alcohol, benzodiazepines, or emerging adulterants such as xylazine or medetomidine. 6. Facilitate seamless linkage to evidence-based treatment. Every overdose or significant nodding-related encounter should provide an opportunity for transition to medications for opioid use disorder (MOUD) and appropriate behavioral health services, without stigma or delay.

Table 1: Policy implications.

Conclusion

Many individuals who use opioids are at high risk for subtle to profound neurological consequences, in addition to well-documented problems associated with OUDs. The use of naltrexone to prevent overdose deaths is launderable, however it does not address the underlying addictive behaviors driving abuse of opioids in society. We believe that futuristic thinking should focus on the root causes of RDS and utilize genetic testing (e.g. GARS) for very early detection of DNA preaddiction liability as well development of non-addicting novel substance/nutraceuticals that induce dopamine homeostasis.

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Author Contribution

The initial draft was developed by KB, KUL and MPL, All co-authors added comments and made significant edits to the manuscript and approved the final manuscript.

Conflict of Interest

KB owns all rights and titles to GARS and KB220.

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