



## Inhalant withdrawal as a clinically significant feature of inhalant dependence disorder

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### SUMMARY

Inhalant use is the intentional inhalation of vapors from commercial products or specific chemical agents for the purpose of achieving intoxication. Inhalants are among the most common and pernicious forms of substance use and the least studied of the major drugs. Diagnosis of inhalant dependence, according to the DSM-IV [Weintraub E, Gandhi D, Robinson C. Medical complications due to mothball abuse. *South Med J* 2000;93:427–9] excludes inhalant withdrawal symptoms, as expert opinion has suggested that an inhalant withdrawal syndrome is neither common nor clinically significant. This article draws from multiple sources of data to suggest that withdrawal symptoms can be part of inhalant dependence and are clinically significant. This hypothesis needs rigorous evaluation to ensure the diagnostic validity of inhalant use disorders.

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### Introduction

Inhalant use is the intentional inhalation of vapors from commercial products or specific chemical agents for the purpose of achieving intoxication [1]. Commonly abused products include gasoline, glue, paint thinner, nail polish, nail polish remover, and spray paint [2]. Numerous specific chemicals may be inhaled including acetone, benzene, butanone, *n*-hexane, and toluene, although varied mixtures of chemicals are found in many abused products [3].

Inhalants are among the most common and pernicious forms of substance use [4,5] and the least studied of the major drugs [6,7]. Inhalant use is associated with harmful outcomes that rival or exceed those characteristic of other drugs of abuse [8,9]. They disproportionately afflict vulnerable subpopulations including the poor, select minority groups, the mentally ill, and persons involved with the juvenile and criminal justice systems [10,11]. Inhalants can lead to “sudden sniffing death” and serious accidents [12–14]. Recent research found that nearly 20% of adults who used inhalants met lifetime criteria for inhalant abuse or dependence [15]. Recent survey evidence also shows widespread use in the adolescent population – that is, approximately 16.1% of 8th graders reported inhalant use, which is slightly higher than the rate of marijuana use among this group (15.7%) [16]. Other survey results show that over one-half million youth aged 12–17 years reported past-year inhalant use [17].

Very little research on inhalant use disorders exists [18]. The general absence of knowledge is reflected in minimal description of inhalant use disorders in the Diagnostic and Statistical Manual, 4th Edition (DSM-IV) [18] vis-à-vis prevalence, course, subtypes, comorbid medical and mental health conditions, and specific age, gender, and sociodemographic features. Moreover, recent findings have raised questions about the reliability and validity of the DSM-IV criteria for inhalant use disorders [19]. This underscores the need for further research on the dimensionality of problematic inhalant use [20] and key signs and symptoms of inhalant use disorders, including tolerance and withdrawal [21–23].

### Inhalant use disorders

Thirteen different classes of psychoactive substances for which abuse or dependence diagnoses exist are defined by DSM-IV [18]. Inhalants represent a distinct class of substances and include both abuse and dependence diagnoses.

#### *Inhalant abuse*

Inhalant abuse is defined using the same set of criteria used for all other substance use disorders – that is, having one or more maladaptive patterns of use that results in clinically significant impairment or distress, including (1) recurrent failure to fulfill major role obligations; (2) recurrent use in physically hazardous situations; (3) recurrent substance-related legal problems; and (4) continued use despite persistent or recurrent social or interpersonal problems due to use [18].

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## Inhalant dependence

Whereas inhalant abuse is defined using the same criteria set used for abuse of other substances, inhalant dependence is defined using a slightly different criteria set than that used for other substances. Specifically, a diagnosis of inhalant dependence requires that three of six dependence criteria be met, whereas other substances with a withdrawal syndrome require that three of seven criteria be met. The six diagnostic criteria for inhalant dependence include: (1) tolerance; (2) substance (inhalant) taken in larger amounts over longer period than intended; (3) a persistent desire or unsuccessful efforts to cut down or control substance (inhalant) use; (4) a great deal of time spent in activities necessary to obtain substance (inhalant) use the substance (inhalant), or recover from its effects; (5) important social, occupational, or recreational activities given up or reduced due to substance (inhalant) use; and (6) substance (inhalant) use is continued despite knowledge of adverse physiological or psychological effects.

Five classes of substances for which a dependence disorder exists do not have a diagnosable withdrawal disorder, including inhalants. In the clinical description of inhalant dependence, the DSM-IV states, "A possible mild withdrawal syndrome has been reported but has not been well documented and does not appear to be clinically significant" [18] (p. 258).

## Hypothesis

Inhalant dependence, as defined by the DSM-IV [18], can include clinically significant withdrawal symptoms that are characteristic of other forms of substance dependence.

## Evaluation

The decision to exclude inhalant withdrawal symptoms from the DSM-IV diagnostic criteria set is based on expert opinion and does not take into account the currently available evidence. For example, a detailed case study of a 21-year-old male reported that he experienced "increased irritability, anxiety, with poor attention and concentration" and "craving" [24] (p. 770) between sessions of inhalant use. Another case report described a 14-year-old boy with "experiences of intense craving [that] interrupted his everyday routine in school and at home" [21] (p. 679). The boy's clinically distressing withdrawal symptoms, both psychological and physiological, persisted for seven days during a hospitalization. The authors of this case report argued that inhalant withdrawal symptoms can be clinically significant among heavy inhalant users, resembling the nature and severity of alcohol withdrawal symptoms.

Ridenour and colleagues [19] reported that inhalant withdrawal was the second most common inhalant dependence criterion among a sample of adolescent inhalant users. A total of 11.1% reported headaches, nausea or vomiting, hallucinations, runny eyes or nose, craving, fast heart beat, depressed mood, and anxiety during withdrawal from inhalants. Other researchers have described an inhalant withdrawal syndrome based on small sample studies, especially those with in-depth comparisons of the phenomenology of inhalant experiences [25]. Comparative studies of clinical presentations for various substances showed inhalants to produce withdrawal symptoms that included restlessness, inattentiveness, anxiety, insomnia, and high levels of craving [26,27].

In addition to studies of human subjects, prior research involving animals in carefully controlled conditions have demonstrated symptoms of physical dependence on and withdrawal from inhalants. For example, in a classic study by Evans and Balster [28], mice were exposed to 1,1,1 – Trichloroethane (TCE), a widely abused solvent. Cessation of 4 days of continuous inhalation of this sub-

stance resulted in a withdrawal syndrome characterized by convulsions. The convulsions diminished 30–60 min following re-exposure to TCE vapor or toluene.

## Conclusion

A stronger knowledge base about inhalant-related symptoms is needed to ensure accurate DSM-IV definitions of inhalant use disorders. This article reviewed clinical, survey and animal studies that imply clinically significant withdrawal symptoms are part of inhalant dependence disorder, and an important step in future research is testing this hypothesis. Moreover, this line of hypothesis testing can lead to a better understanding of the clinical course of inhalant use disorders, which will greatly aid in developing evidence-based treatments and aiding treatment selection. This is particularly important given that no evidenced-based treatments for inhalant use disorders exist. Without this knowledge, inhalant users may be at risk of being misdiagnosed and face restricted access to treatment, and interventions for inhalant use disorders will not adequately address the full range of clinical needs.

## Conflict of interest statement

None declared.

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