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Substance-Induced Mood Disorders: A Scoping Review

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Abstract

Purpose of the Review Substance-induced mood disorders (SIMDs) are an understudied area with a limited published literature. This scoping review evaluated published evidence to determine differences between SIMDs and independent mood disorders with comorbid SUD.

Recent Findings Following Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines, English language articles were searched through October, 2023. Thirty-one studies were identified which explored the relationship between alcohol, cocaine, opioids, methamphetamine, cannabis, and multiple substance use and the induction of mood disorders. Varying symptoms and risk factors were identified for SIMD, specifically for alcohol and opioids. However, confounding factors and heterogeneity in the majority of studies make it difficult to establish clear differences between these groups.

Summary Although our findings suggest risk factors and symptoms that may be implicated in SIMD, results are inconsistent. Further research using well-controlled, experimental, and longitudinal designs are needed to parse differences between SIMDs and comorbid mood disorders with SUDs.

Keywords Substance-Induced Mood Disorder · Major Depression · Bipolar Disorder · Co-Morbidity · Treatment

Introduction

Substance-Induced Mood Disorders (SIMDs) are a distinct category of mood disorder in patients that misuse addictive substances [1]. The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) defines these as "a prominent and persistent disturbance of mood…that is judged to be due to the direct physiological effects of a substance (e.g., an addictive drug, a medication, or somatic treatment for depression, or toxin exposure)" [1]. There have been recent changes to the diagnostic criteria for SIMDs as the DSM-5 (Test Revision, TR) was edited to enhance its clarity and consistency [2]. Changes to the DSM-5-TR include eliminating "mood disorders" in favor of "bipolar and related disorders" grouping and a "depressive disorders" grouping [2]. SIMDs typically present during a period of intoxication from the substance or while experiencing withdrawal from the substance [1]. Clinically, SIMDs do not present as diagnoses of long duration as compared to that of independent mood disorders and the condition typically reverses with acute abstinence from the substance. Independent mood disorders may be diagnosed as a major depressive episode, major depressive disorder (MDD), dysthymic disorder, cyclothymic disorder, (hypo)manic episode, bipolar I disorder or bipolar II disorder, with a concurrent substance use disorder (SUD) [1]. Independent mood disorders can be diagnosed using the DSM-5, which differ from SIMD in the lack of requirement for substance use to be a criterion with a focus on the emotional state of an individual and its interference with their ability to function. SUDs can be diagnosed with the DSM-5 as well using a set of eleven criteria, with disease severity ranging as mild to severe. Two nationally representative large-scale surveys, including the National Epidemiologic Survey on Alcoholism and Related

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Conditions (NESARC), which surveyed 43,093 people in 2001 and 2002 [3, 4], and the National Comorbidity Survey (NCS) Replication, which surveyed 9,282 people in 2001 and 2003 [5, 6] collected data on the prevalence of mood disorders, SUDs, and their comorbidities. The lifetime prevalence of any bipolar disorder and any SUD is 47.3%, whereas for bipolar I disorder, and any SUD is 60.3%. Additionally, comorbid SUD also presents at high prevalence in major depression with lifetime rates of 40.3% for any alcohol use disorder and 17.2% for any drug use disorder [7]. Other research highlights the lifetime prevalence of substance-induced depressive disorders to be between 0.26% and 1%, in which the top substances involved with the induction of depression are alcohol and opioids [1]. Compared to MDD, in which the lifetime diagnosis is 13.2–16.6%, the rates are vastly different [7]. These numbers are very likely an underestimate. The cerebral cortex and subcortical areas such as the limbic system, thalamus, hypothalamus, and basal forebrain are especially vulnerable to alcoholism-related damage [8]. Alcohol can disrupt brain neurochemistry, including glutamate, gamma-aminobutyric acid (GABA), serotonin (5-HT), endogenous opioid peptide (EOP), and dopamine (DA) neurotransmission [8, 9]. Anhedonia, the inability to feel pleasure, has been linked to dysfunction of the dopamine reward system [10]. Nonetheless, the pathophysiology of SIMDs remains a topic of ongoing discussion [10, 11]. Clinically, treatment response may differentiate between primary mood disorders patients and SIMD as previous meta-analyses have reported a lack of SSRI response in patients with comorbid depression and substance use, possibly contributing to the presence of substance-induced depression as a confounder in the samples [12, 13]. Clinically, treatment for patients with SIMD may vary as results have shown antidepressants may not always improve depression. However, reductions or abstinence from drinking (and other substance use) typically improves depressive symptoms [14]. This scoping review evaluates the current literature published on identifying key characteristics of SIMDs versus independent mood disorders, and how to successfully manage these distinct disorders.

Methods

Search Strategy

Following Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines, original, peer-reviewed articles published from database inception to October, 2023 were searched for using PubMed, Google Scholar, ProQuest, Ovid, and PsycINFO [15]. Databases were searched using the following terms: ("cannabis-induced" OR "marijuana-induced" OR "weed-induced" OR "cannabinoid-induced" OR "alcohol-induced" OR "opioid-induced" OR "substance-induced" OR "stimulant-induced" OR "substance-related") AND ("mood disorder" OR "depression" OR "anxiety" OR "bipolar disorder" OR "major depressive disorder"). Titles and abstracts were screened for relevance by three of the authors (AK, CW and AP), and full-text reviews were conducted for eligibility by AK, CW and AP, where disagreements were resolved through consensus between the three authors or through consultation with the senior author (TPG). Covidence software was used to collate search results.

Studies were included if they were: 1) longitudinal, cross-sectional, experimental, or retrospective; 2) included a sample demonstrating substance use at baseline; 3) utilized a validated or objective measure to establish diagnosis of mood disorder (e.g. DSM-III, DSM-IV, DSM-5); and 4) utilized a validated measure to establish substance use (e.g., self-report, urine screens, previous drug reports, structured interviews). Exclusions were publications that were reviews, meta-analyses, and case studies.

Risk of Bias

The quality of longitudinal and cross-sectional studies was assessed using the Newcastle Ottawa Scale (NOS). The rating system has a 9-point grading scale that measures the following domains: (1) the selection process; (2) comparability of patients based on design; (3) outcome assessment. To ensure only methodologically sound studies were included in this review, we included only publications that received a score ≥ 5.

Results

A total of 1,051 articles were identified from the initial search and a subsequently 999 were excluded based on initial inspection of the titles and abstracts using Covidence software. After title and abstract screening, 52 articles were read in full and assessed for eligibility. 21 articles were excluded, leaving 31 articles included for evaluation (See PRISMA Diagram; Fig. 1).

Study Characteristics

One study was an observational cohort, one a pilot study, one was a randomized controlled trial, fourteen studies employed cross-sectional designs, eight utilized retrospective methods, one applied case–control methods, and four were longitudinal (See Table 1). These included $N = 75{,}158$ participants, with sample sizes ranging from 42 to 43,093. Substances studied linked to onset of mood disorders evaluated included opioids, alcohol, cocaine, methamphetamine, cannabis, and polysubstance use.

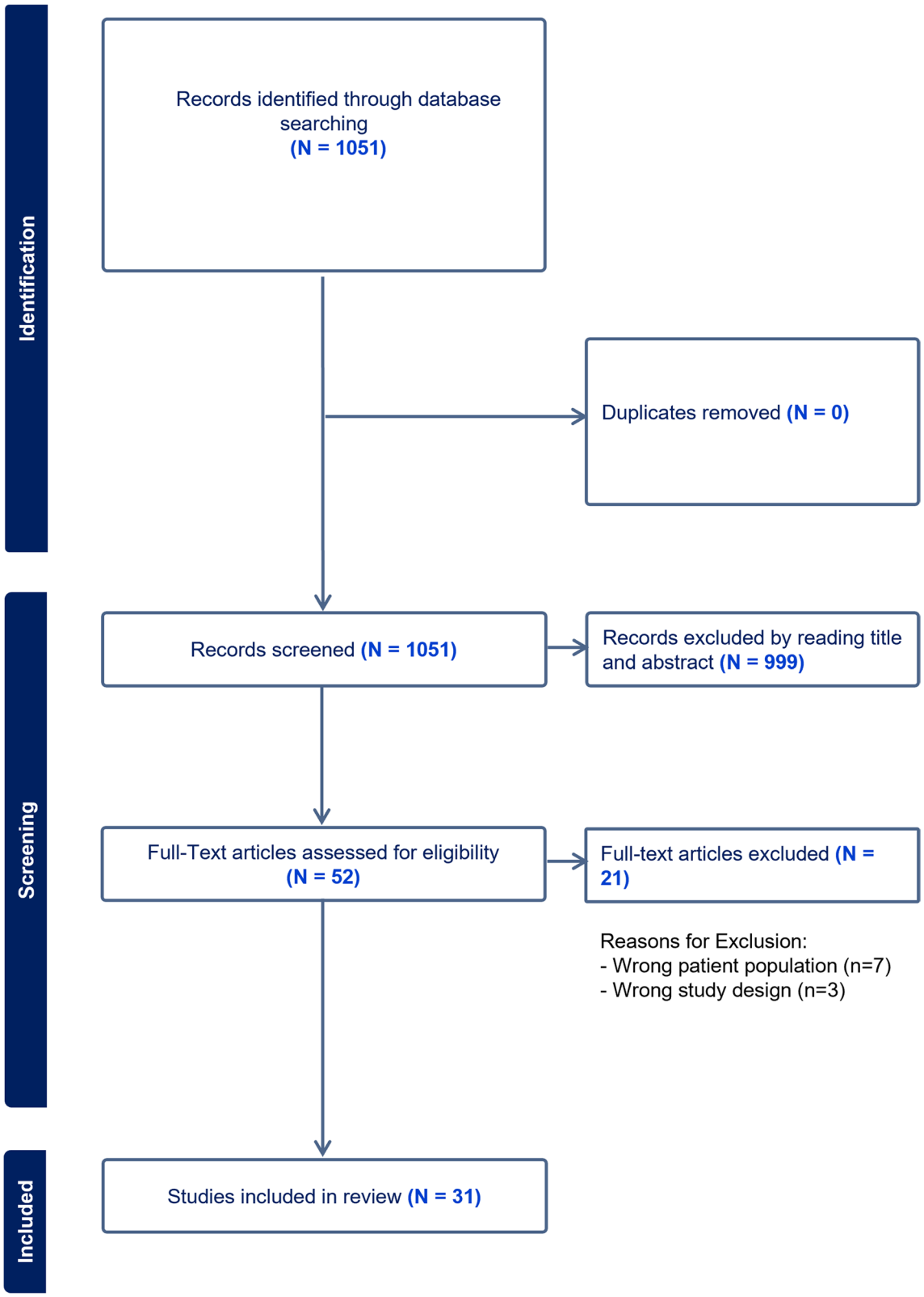

Fig. 1 PRISM-A diagram for study selection

Table 1 Studies included in scoping review of Substance-Induced Mood Disorders (SIMDs)

Studies ($N=31$)	Sample Size ($N=75,158$)	Substance Evaluated	Psychiatric Diagnosis	Measured Outcomes	Study Design	Results	NOS Rating
Opioids ($n=5$ studies, 2,441 Participants)							
Ahmadi et al., 2005 [20]	$n=500$ opioid-dependent participants	Opioids	Mood & anxiety disorders through DSM-IV	DSM-IV diagnosis of mood and anxiety disorders	Observational cohort study	54.8% of participants were diagnosed with substance-induced depression and 21% with substance-induced anxiety disorder, making these the most prevalent mood and anxiety disorders, respectively, in the sample.	6
Ahmadi et al., 2004 [16]	$n=500$ opioid-dependent outpatients	Opioids	MDD & BPD through DSM-IV and SCID	DSM-IV and SCID	Cross-sectional interview-based study	274 of the 500 outpatients were diagnosed with substance induced depression.	6
Ahmadi & Ahmadi, 2005 [17]	$n=500$ opioid dependents seeking treatment	Opioids	Anxiety and depression via DSM-IV	DSM-IV	Cross-sectional interview-based study	105 individuals had SI- anxiety disorder and 274 had SI-depression.	6
Mackesy-Amiti et al., 2012 [18]	$n=570$	Opioids	SUD and psychiatric disorders (SI-MDD, SI-dysthymia, SI-Panic disorder, SI-GAD, SIP) through DSM-IV	PRISM, DSM-IV	Cross-sectional descriptive interview-based study	Most past year episodes of major depression and dysthymia were substance-induced. Less than half ($N=59$, 44%) of participants with past year substance-induced major depression had received treatment.	7
Mowla et al., 2008 [19]	$n=371$ male patients	Opioids	MDD through HAMD and DSM-IV	DSM-IV, HAMD-21, Beck Hopelessness Scale	Retrospective qualitative study	OID patients were rated on the HAMD-17 as significantly more depressed ($Z=3.594$, $P=0.000$) item 1 depressed mood), item 4 (early insomnia), item 7 (work and activity), item 8 (psychomotor retardation), item 12 (gastrointestinal symptoms and anorexia), item 14 (genital symptoms), item 15 (hypochondrias), and item 17 (insight) differed significantly between groups with substance- induced depressed patients scoring worse ($p<0.05$).	7

Table 1 (continued)

Studies ($N=31$)	Sample Size ($N=75,158$)	Substance Evaluated	Psychiatric Diagnosis	Measured Outcomes	Study Design	Results	NOS Rating
Alcohol ($n=6$ studies, 43,748 Participants)							
Blanco et al., 2012 [26]	$n=43,093$ adults from the NESARC ($N=3308$ MDD-NSUD, $N=2387$ MDD-SUD, $N=106$ SIDD)	Alcohol	Major depressive disorder (MDD), substance-induced depressive disorder (SIDD) via AUDAIDIS-IV	Alcohol Use Disorder and Associated Disabilities Interview Schedule—DSM-IV Version (AUDADIS-IV)	Retrospective Cohort Study	The lifetime prevalence of SIDD in the general population was 0.26%. In terms of rates of MDD risk factors, likelihood of experiencing a comorbid psychiatric disorder, and number of DSM-IV MDD criteria met, SIDD and MDD-SUD demonstrate similar rates, which were greater than those seen in MDD-NSUD. Compared to MDD-SUD and MDD-NSUD, SIDD experience fewer depressive episodes on average and seek treatment more, but they were also more likely to self-medicate MDD using alcohol/substances and less likely to receive medication.	9
Conner et al., 2014 [27]	$n=100$ cases (patients at a SUD treatment program who had attempted suicide), $N=100$ controls (from the same treatment site but no history of suicidal thoughts/attempts)	Alcohol	Substance-induced depression (SID) via PRISM	Self-reported suicide attempt, assessment of suicide planning, Suicide Intent Scale, PRISM, AUDIT, Drug Abuse Screening Test, Lifetime History of Aggression Questionnaire, presence/absence of child sexual abuse, semi structured stressful life-event interview	Case–control observational study	SID was more prevalent than independent depression, with 60% of cases and 35% of controls having SID compared to 13% of cases and 3% of controls having independent depression. SID was associated with increased risk of suicide attempt compared to nondepressed participants (AOR = 3.73) but there was no statistically significant difference between risk for attempt between SID and independent depression (AOR = 2.78). Still, independent depression trended towards conferring greater attempt risk than SID ($p=0.17$).	7

Table 1 (continued)

Studies ($N=31$)	Sample Size ($N=75,158$)	Substance Evaluated	Psychiatric Diagnosis	Measured Outcomes	Study Design	Results	NOS Rating
Kahler et al., 2002 [28]	$n=166$ patients admitted to alcohol and drug treatment unit	Alcohol	MDD via DSM-IV	BDI, DSM-IV, SCID-P, Dysfunctional Attitude Scale, Self-control scale, TLFB	Cross-sectional study	69 participants had SIMDD, of which 38 previously had an episode of SIMDD. Those in the SIDD group with a history of past substance-induced MDD reported greater use of ineffective coping (Mean [SD]=0.18 [0.82]) than those who did not have a history of past substance-induced MDD (Mean=-0.37 [0.99]) ($p=0.013$).	7
Ramsey et al., 2004 [29]	$n=95$ patients undergoing treatment	Alcohol	MDD through DSM-IV and BDI scores	DSM-IV, SCID, BDI	Longitudinal treatment outcome study	Patients whose diagnoses were reclassified had significantly lower Alcohol dependence scale (ADS) scores and were significantly more likely to have a history of independent MDD relative to those whose diagnoses were not changed. The adjusted odds ratio of 5.26 ($p=0.006$) for history of past independent MDD indicated a greater than fivefold increase in the odds of diagnosis change compared with those without a past independent MDD diagnosis.	8

Table 1 (continued)

Studies ($N=31$)	Sample Size ($N=75,158$)	Substance Evaluated	Psychiatric Diagnosis	Measured Outcomes	Study Design	Results	NOS Rating
Simpson et al., 2022 [31]	$n=101$ alcohol dependent participants	Alcohol	PTSD via DSM-5	Comparison of a PTSD treatment (Cognitive Processing Therapy (CPT)), an AUD treatment (Relapse Prevention (RP)) and an assessment only (AO) for those meeting diagnostic criteria for both PTSD and AUD	Parallel group, randomized clinical trial	At post-treatment, participants assigned to CPT showed significantly greater improvement than those in AO on PTSD symptom severity. CPT and RP significantly decreased heavy drinking days relative to AO. After re-randomization both treatment conditions showed substantial improvements in PTSD symptoms and drinking between pre-treatment and post-treatment over the 12-month follow-up period, with RP showing an advantage on heavy drinking days.	7
Gallagher et al., 2018 [32]	$n=93$ alcohol dependent participants	Alcohol	Anxiety and depressive symptoms	Symptoms of anxiety, depression, and general psychosocial functioning and Alcohol Use Disorder	Longitudinal observational study	Significant improvements in symptoms of anxiety and depression after 28 days of treatment for alcohol dependence.	8
Cocaine ($n=2$ studies, 5,692 Participants)							
Vergara-Moragues et al., 2012 [24]	$n=227$	Cocaine	Mood, anxiety, psychotic, and eating disorders, and two Axis II disorders, borderline and antisocial personality disorders through DSM-IV-TR	PRISM, DSM-IV-TR	Cross-sectional study	Substance-induced mood (21.6%) and psychotic (11.5%) disorders were more prevalent in this population than independent mood (12.3%) and psychotic (7.5%) disorders.	7
Zarkowski et al., 2007 [25]	$n=5465$	Cocaine	Excessive crying/tears as marker of MD	Urine toxicology	Retrospective case record study	The prevalence of the sign in the general population was 1.9%. Patients with excessive tearfulness were more likely to have cocaine in their urine ($P<0.0001$), receive a substance-related primary diagnosis ($P<0.0001$), and be admitted for psychiatric hospitalization ($P<0.001$).	6

Table 1 (continued)

Studies ($N=31$)	Sample Size ($N=75,158$)	Substance Evaluated	Psychiatric Diagnosis	Measured Outcomes	Study Design	Results	NOS Rating
Methamphetamine ($n=2$ studies, 589 Participants)							
McKetin et al., 2011 [22]	$n=400$	Methamp-hetamine	MDD through DSM-IV	CIDI, SF-12, OTI, DSM-IV	Cross-sectional interview-based study	176/400 patients had SI-MDD. This substance-induced depression had a similar symptom profile to major depression, but with lower levels of suicidal ideation and with fewer participants reporting depressive symptom episodes that lasted 2 weeks or more ($p<0.01$).	8
Salo et al., 2011 [23]	$n=189$	Methamp-hetamine	MDD, bipolar disorder, Depression NOOS, Dysthymia through DSM-IV & SCID	DSM-IV, SCID	Cross-sectional qualitative study	Mood and anxiety disorders were less often substance-induced than not substance-induced (15% vs. 32% and 4% vs. 24%, respectively). There was a significant difference between men and women in the prevalence of MA-induced delusional disorder (24 [19.0%] versus 1 [1.5%]; p = 0.0004, two-tailed Fisher's exact test)	7
Cannabis ($n=1$ study, 7,735 Participants)							
Van Laar et al., 2007 [21]	$n=7735$	Cannabis	Mood and anxiety disorders through DSM-III-R & SCID	DSM-III-R, CIDI	Retrospective study from NEMESIS survey	Any use of cannabis at baseline predicted a modest increase in the risk of a first major depression (odds ratio 1.62; 95% CI, 1.06–2.48) and a stronger increase in the risk of a first bipolar disorder (odds ratio 4.98; 95% confidence interval 1.80–13.81)	8

Table 2 Effects of Multiple Substances on Induction of Mood Disorders ($n = 14$ studies, 14,953 Participants)

Bakken et al., 2003	$n = 287$ substance-dependent/SUD participants	Alcohol, opioids, cannabis, sedatives/hypnotics, cocaine, amphetamines, hallucinogens, inhalants	Psychiatric Axis I disorders (substance-induced disorders, mood disorders, anxiety disorders, somatoform disorder, eating disorder) through CIDI	Composite Internation-al Diagnostic Interview (CIDI) diagnosis of Axis I disorders	Retrospective cohort study	42% of all participants had both substance-induced and substance-independent mental disorders, while 5% had only substance-induced mental disorder(s). In total, nearly half (47%) of participants had a SIMD. The primary SUD group more frequently had substance-induced mental disorders than the secondary SUD group, but this difference was nonsignificant after controlling for gender.	6
Dakwar et al., 2011	$n = 176$ individuals with lifetime independent depression or substance-induced depression	Cocaine, cannabis, opioids	Substance-induced depression (SID) through DSM-IV-TR & HAMD	Structured clinical interview for DSM-IV-TR disorders (SCID), Hamilton depression scale (HAMD)	Observational cohort study	Compared to those with independent depression, individuals with SID were less likely to be female (24.2% vs. 40.3%, $p < 0.05$), and they had lower HAMD scores (10.4 vs. 16.2, $p = 0.002$), lower prevalence of comorbid PTSD (5% vs. 12.5%, $p < 0.05$), lower prevalence of cannabis dependence (19.7% vs. 55.7%, $p < 0.001$), and higher prevalence of cocaine dependence (48.4% vs. 24.4%, $p < 0.001$).	7
Fabricius et al., 2008	$n = 239$ individuals with co-occurring substance-related and psychiatric disorders (CODs)	Alcohol, cocaine, cannabis, opioids, amphetamines, sedatives/hypnotics/anxiolytics, hallucinogens	Mood disorder	Interview data	Retrospective cohort study	Mood disorders were significantly associated with being substance-induced ($p < 0.0001$).	6

Table 2 (continued)

Garlow et al., 2003	$n=777$	Alcohol, cocaine, SUD	SIMD from cocaine use disorder, AUD, cocaine and AUD	Suicidal ideation	Retrospective case sample from PES hospital unit	Over 52% of patients with substance induced depression expressed suicidal ideation ($p<0.0001$). Of this, 85% of patients with a SIMD attributed suicidal ideations to the effects of cocaine ($p<0.0005$).	8
Herrero et al., 2008	$n=139$	Cocaine and heroin	Mood and anxiety disorders	SIMD vs comorbid MD and CUD	Cross-sectional study	22 subjects were diagnosed with a substance induced disorder (10.8% SIMD & 2.2% substance induced anxiety). Substance-induced disorders were more likely to have been previously treated for substance use compared to primary disorder patients (OR: 8.438 (1.172–60.776) $p<0.05$).	8
Langas et al., 2012	$n=61$	Alcohol and 'drugs'	Mood disorders and substance use disorders via DSM-IV, AUDIT, and DUDIT	Symptom Checklist-90-Revised, the Inventory of Depressive Symptoms, the Montgomery Asberg Depression Rating Scale, the Young Mania Rating Scale, and the Angst Hypomania Check List, DSM-IV-TR, AUDIT, DUDIT	Cross-sectional descriptive diagnostic study and a comparative study	Of the 61 patients, only 4 had substance-induced disorders.	8
Langas et al., 2013	$n=42$	Alcohol and drugs	MDD through DSM-IV	AUDIT, CUDIT, PRISM, DSM-IV, SCID	Cross-sectional descriptive study	10/42 patients had SI-MDD. found more insomnia and concentration problems in independent MDD (p=0.008 & 0.001, respectively).	8

Table 2 (continued)

Magidson et al., 2013	$n = 2{,}121$	Alcohol, nicotine, 'drugs'	MDD through DSM-IV	DSM-IV, AUDADIS-IV,	Cross-sectional follow-up to a longitudinal	Among individuals diagnosed with SIDD at Wave 1 ($n = 88$), 71.27% were reclassified as having no depressive episode at Wave 2, 27.32% were reclassified as having an independent MDD episode, only 0.77% were again classified as having SIDD, and 0.64% were classified as having had both SIDD and an independent MDD episode.	9
Niciu et al., 2009	$n = 1929$	Alcohol, cocaine, or opioids	No lifetime MDE (no MDE), independent MDE only (I-MDE), substance-induced MDE only (SI-MDE) and both types of MDE via SSADDA & DSM-IV	SSADDA, DSM-IV	Cross-sectional qualitative study	Subjects with both types of MDE reported more life-time depressive symptoms and comorbid anxiety disorders and were more likely to have attempted suicide than subjects with I-MDE or SI-MDE. Subjects with both types of MDE, like those with I-MDE, were also more likely than subjects with SI-MDE to be alcohol-dependent only than either drug-dependent only or both alcohol- and drug-dependent.	7

Table 2 (continued)

Nunes et al., 2006	$n = 110$	Alcohol, cocaine, opioids	MDD through DSM-IV	DSM-IV, PRISM	Longitudinal observational study	Depression during follow-up was equally likely among patients with current (baseline) DSM-IV independent or substance-induced MDD; in the latter group, past independent MDD increased the likelihood of MDD during the follow-up. 56 (51%) were diagnosed as having current substance-induced MDD (C-SI-MDD).	7
Samet et al., 2013	$n = 250$	Cocaine, heroin, and/or alcohol dependence	Major depression through DSM-IV	DSM-IV, PRISM	Longitudinal observation study	Substance-induced major depression significantly predicted post-discharge use of alcohol, cocaine, and heroin (hazard ratios 4.7, 5.3 and 6.5, respectively). Substance-induced MDD also adversely affected the chances of remission from heroin dependence (HR: 0.1).	7
Schuckit et al., 2007	$n = 2548$ patients from the SSAGA-IV study	Alcohol and 'illicit substances'	MDD through DSM-IV	DSM-IV	Retrospective study	Those with substance-induced depressions (Group 2) were more likely to be original alcoholic probands, be males, be non-white, and have less education. They were also more likely to have alcohol, drug, or antisocial personality diagnoses and to report higher maximum drinks. However, symptoms during the worst depressive episode were quite similar across Groups 1 and 2.	7

Table 2 (continued)

Some et al., 2022	$n=6021$	Alcohol and cannabis	Symptoms of anxiety and depression through GAD-7 & CES-D, respectively, symptoms of loneliness	GAD-7, CES-D, self-reported interview	Cross-sectional web-based interview	Individuals in the high-symptom class were more likely to use cannabis at least once a week (aOR = 2.28, 95%CI:1.92–2.70), drink alcohol heavily (aOR = 1.71, 95%CI:1.49–1.96); and increase the use of cannabis (aOR = 3.50, 95%CI:2.80–4.37) and alcohol (aOR = 2.37, 95%CI:2.06–2.74) during the pandemic.	7
Thomasius et al., 2005	$n=118$	Ecstasy and polydrug users	Axis I disorders through DSM-IV	DSM-IV	Cross-sectional qualitative study	Six current ecstasy users, four ex-ecstasy users and one polydrug control had suffered from a substance-induced anxiety disorder in their lifetime (present diagnosis: $P=0.049$; life-time diagnosis: $P=0.153$). The disorders had been induced by ecstasy in three cases, cannabis in two cases, LSD in two cases, cocaine in one case and multiple substance use in three cases.	8

Table 2 (continued)

Taylor et al., 2022	*N* = 135 homeless participants	Alcohol and illicit substance use	PTSD		Alcohol and illicit substance use severity and PTSD symptom severity	Pilot study	Mental Health service was associated with a significant reduction in alcohol and illicit substance use severity but was not associated with changes in PTSD symptom severity. The overall sample showed a significant improvement at 12 months in alcohol use severity, illicit substance use severity and PTSD symptoms.	6

Opioids-Induced Mood Disorders (*n* = 5)

Five studies [16–20] evaluated the role of opioids in the onset of mood disorders, with all finding a temporal correlation of opioid use to the induction of major depressive disorder, dysthymia, or anxiety (Table 1). Importantly, three studies used the same data set yet evaluated different outcomes [16, 17, 20]. One study evaluating 500 treatment-seeking opioid-dependent patients found that 274 (54.8%) were diagnosed with substance-induced depression and 105 (21%) of individuals were diagnosed with substance-induced anxiety [16, 17]. All patients involved in the studies reported using opioids for a duration of 1–5 + years, with over 86.4% of the sample reporting a daily use between 1–5 g/day. Mowla and colleagues conducted a retrospective study comparing the symptoms of independent major depressive disorder (MDD) with that of opioid-induced depression (OID) using the Hamilton Depression Rating Scale (17-item) (HDRS-17) and BDI Hopelessness Sub-Scale in a group of male patients [19]. Overall scores on the HAMD-17 were significantly higher for OID patients, including depressed mood, early insomnia, activities, psychomotor retardation, gastrointestinal symptoms and anorexia, genital symptoms, hypochondrias and insight differed significantly, with OID patients having higher scores (all p's < 0.01) [19]. Although patients included in the study were not using any kind of substance or psychotropic medication in the past six months, all patients included were treatment-seeking.

Cannabis-Induced Mood Disorders (*n* = 1)

Only one study [21] evaluated cannabis regarding the induction of mood disorders (Table 1). A retrospective study evaluated the results from the Netherlands Mental Health Survey and Incidence Study (NEMESIS), which employed in-person interviews using the Composite International Diagnostic Interview (CIDI) [21]. When adjusting for alcohol and other substance use disorders, lifetime psychotic symptoms, and lifetime anxiety disorders using self-reported cannabis frequencies of 1–3 days a month, 1–4 days a week, and almost every day produced odds ratios (ORs) of 1.38 (CI: 0.70–2.71), 2.57 (CI: 1.33–4.98), and 2.38 (CI: 1.09–5.19), respectively to the subsequent diagnosis of any mood disorder. Additionally, controlling for the same confounders, a non-significant OR of 1.18 (CI: 0.71–1.97) was found for any anxiety disorder at 3-year assessment.

Methamphetamine-Induced Mood Disorders (*n* = 2)

Two cross-sectional studies [22, 23] investigated methamphetamine-induced mood disorders. One study evaluated

400 methamphetamine-treatment seeking participants, in which 176 were diagnosed with substance-induced depression (SID) [22]. Similar symptoms profiles for SID patients and independent MDD patients were observed; however, SID patients reported lower rates of suicidal ideation and depressive symptom episodes lasting at least 2 weeks. Interestingly, 66/176 (37.5%) had polydrug use, which was not controlled for in the analysis, but results were adjusted for other substances, including cannabis [OR 2.4 (CI: 1.2–4.6, p = NS)] and benzodiazepines [OR 2.0 (CI:1.0–4.0; p = 0.049)] [22]. In another study evaluating 189 methamphetamine-dependent subjects, the prevalence of independent mood, psychotic, and anxiety disorders was determined [23]. Of the participants included, 20/189 (10.6%) were diagnosed with a lifetime methamphetamine-induced mood disorder and 7/189 (3.7%) with a lifetime methamphetamine-induced anxiety disorder, while 61 (32.3%) were diagnosed with an independent mood disorder not caused by substance use [23]. Notably, demographic variables were controlled for, but the use of other substances was not.

Cocaine-Induced Mood Disorder (*n* = 2)

Two studies evaluated cocaine-induced mood disorders [24, 25]. Vergara-Moragues and colleagues used the Psychiatric Research Interview for Substance and Mental Disorders (PRISM) to determine current and lifetime diagnoses of SIMDs. Thirty-one (13.7%) participants had a current diagnosis of cocaine-induced mood disorder, and 10 (4.4%) participants had a current diagnosis of cocaine-induced anxiety disorder [24]. This was compared to lifetime diagnosis where 49 (21.6%) of SIMD and 12 (5.3%) were diagnosed with a substance-induced anxiety disorder. Although other substances and past psychiatric history were not controlled for, 63.3% of patients had reoccurring SIMD and 83.3% had reoccurring substance-induced anxiety disorder [24]. Interestingly, when trying to identify symptoms that may be attributed to cocaine-induced mood disorders, Zarkowski and colleagues found that in a group of psychiatric emergency services patients, 36 (1.9%) showed excessive tears and were more likely to receive a primary diagnosis of SIMD and were twice as likely to be admitted for inpatient care ($P < 0.001$) [25]. Although 65% of patients with excessive tearfulness were positive for cocaine in their urinalysis, controlling for other substance use or previous psychiatric history was not performed.

Alcohol-Induced Mood Disorders (*n* = 4)

The largest study in this area of alcohol-induced mood disorders was a retrospective epidemiologic study completed by Blanco and colleagues, which showed that the lifetime prevalence of SID was 0.26% [26]. Moreover, these patients were more likely to self-medicate using alcohol and less likely to receive medication for depressive symptoms [26]. When examining suicide attempts in patients with alcohol use disorder, SID was diagnosed in 60% of attempters and 35% of controls, whereas independent depression was diagnosed with in 13% of attempters and 3% of controls (suicide attempt risk SID OR: 3.73) [27]. Additionally, alcohol-induced mood disorders typically present as episodic events, not chronically. Individuals with recurring SIMD showed more problematic coping strategies compared to those with a first-time diagnosis [28]. Importantly, a diagnosis of SIMD can transition into independent MDD even when abstinence is achieved [29]. In patients with a previous history of MDD, there is a five-fold increase in the odds of changing diagnoses compared to individuals with no history of MDD (OR: 5.26, P = 0.006) [29]. Furthermore, approximately 12% of individuals with lifetime alcohol use disorder (AUD) have lifetime PTSD [30]; a recent study compared treatment strategies for people with AUD and comorbid posttraumatic stress disorder (PTSD). It was found that treatments targeting only AUD or only PTSD still have salutary effects on both PTSD and drinking outcomes [31]. Another study by Gallagher et al. also confirmed significant improvements in symptoms of anxiety and depression after 28 days of treatment for AUD [32].

Polysubstance-Induced Mood Disorders (*n* = 14)

Fourteen studies [33–46] evaluated polysubstance-induced mood disorders (Table 2). Given the heterogeneity in these studies, it is difficult to attribute certain substance effects to the diagnosis of a particular SIMD. Mood and anxiety disorders, among other psychiatric diagnoses, are associated with an increased risk of substance use [47]. For individuals using multiple substances, clinical symptomatology may present differently in this group; there is evidence predicting increased relapse to substance use after treatment in these patients [43]. However, it has been shown that homeless individuals seeing a mental health professional is associated with a significant reduction in alcohol and illicit substance use, but not necessarily with lower psychiatric symptom severity [48]. Additionally, individuals presenting with more severe symptoms were likely to use cannabis at least once a week (aOR = 2.28), drink alcohol heavily (aOR = 1.71), and increase use of cannabis (aOR = 3.50) and alcohol (aOR = 2.37) during the study period [45].

Discussion

This review evaluated the use of various substances in the induction of mood disorders versus co-occurring mood disorders and SUDs, with emphasis on differentiating the symptomatology, course and treatment strategies between these groups (see Fig. 2). The published lifetime prevalence of SIMD is low at 0.26–1.0% [1], and probably underestimated. The findings of this review suggest a temporal relationship between the use of substances and the induction of a mood disorder, which may present with highly variable symptoms compared to independent mood disorders. Of the substances evaluated in the included studies, opioids and alcohol have the highest prevalence with respect to SIMDs. Moreover, tobacco was identified in multiple populations but did not significantly contribute to the results of these studies. When quantified, heavy substance use was positively correlated with a diagnosis of SIMD; however, evidence for dose-dependent relationships were limited. Another important trend observed across various substances was the reoccurring diagnosis of SIMD. Patients with a previous diagnosis of SIMD were more likely to have a repeated diagnoses of SIMD compared to patients without SIMD history. Numerous studies evaluated treatment-seeking patients and found that individuals with a SIMD were more likely to seek treatment for their substance use compared to independent mood disorders with co-occurring SUDs. Where studies evaluated suicidal ideation and attempts, individuals with a SIMD had a higher prevalence of suicide attempts compared to independent mood disorders.

Study Strengths and Limitations

While varying symptomatology and potential risk factors were identified in this review, the results need to be interpreted with caution due to certain methodological limitations. Although 29 papers with NOS scores ≥ 5 were included in this review, 14 papers evaluated the use of multiple substances in the induction of mood disorders or a cohort of heterogenous participants in which multiple substances were included. Thus, it is difficult to interpret the results of these polysubstance use studies (Table 1). Moreover, studies evaluating the use of a single substance did not always control for polysubstance use. Finally, sample sizes of studies evaluating single substances were modest. Thus, studies of SIMD across substances require larger sample sizes, controlling for confounding substance use.

Clinical Implications

It is important to acknowledge the studies included identifying individual substances are limited, which may minimize clinical applicability. The results of this review emphasis the need for accessible treatment for problematic substance use to prevent SIMDs, and integrated treatments for both the substance misuse and associated mood disorder (including antidepressant and mood stabilizers). Moreover, clinicians should properly assess patients seeking treatment that present symptoms of a mood disorder, even when no prior history of a mental health disorder is present, with an index of suspicion for co-occurring SUDs. Clinicians should be aware of the impacts that substances may have on mental health outcomes, and should be aware of the differentiation between independent and SIMDs.

Conclusions and Future Directions

Our findings suggest that there may be differential presentations between SIMDs, and independent mood disorders with co-occurring SUDs. Due to the extremely low rates of lifetime SIMDs diagnosed in the general population, it appears that SIMD diagnoses are significantly underestimated. While it is known that mood disorders and SUDs commonly occur

Fig. 2 A comparison of primary mood disorders with SUDs versus Substance-Induced Mood Disorders (SIMDs)

Primary Mood Disorders with SUDs	Substance-Induced Mood Disorders (SIMDs)
Onset prior to substance use	Related to the active use, intoxication, or withdrawal from substances
Commonly associated with factors independent of substance use	Commonly associated with heavy substance use
Variable timing in resolution of symptoms, sometimes with partial resolution	Symptoms resolve following cessation of heavy substance use or acute withdrawal in less than one week
Mood symptomatology independent of substance use	Mood symptomatology is causally related to substance use
Positive laboratory test of substance use present in some patients	Positive laboratory test of substance use present in all patients
Antidepressant markedly improve symptoms	Unclear if antidepressant or mood stabilizers alleviate symptoms

together, with negative impacts on illness course, very little research has been done to understand the mechanisms and clinical features of SIMDs versus dual disorders. With increasing recreational use of substances (e.g. cannabis, stimulants, opioids) and decreased perceptions of risk, the need for continued experimental and longitudinal research to clarify the scope and impacts of SIMDs are warranted [49]. Furthermore, high-quality studies are needed to investigate risk factors, symptoms, and effective treatments for SIMDs with stimulant, cannabis, alcohol, opioid and other SUDs, as well as integrated treatments for substance misuse and induced mood disorders.

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Declarations

The Section Editors for the topical collection Dual Diagnosis are Tony George and Victor Tang. Please note that Section Editor Tony George was not involved in the editorial process of this article as he is a co-author.

Conflict of Interest Dr. George reports consulting work with Roche, Frutarom and Sanford Burnham Prebys in the past three years. He serves as Co-Principal Editor of Neuropsychopharmacology (NPP) and as Chair, Scientific Advisory Committee for the Canadian Centre on Substance Use and Addiction (CCSA).

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