Psychopathology of dual diagnosis: new trumpets and old uncertainties

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Summary

People suffering from severe mental illnesses, such as schizophrenia and major affective disorders, have high rates of addictive behaviours related to alcohol and illicit substance use. This overview summarises new and old psychopathological issues on the comorbidity between mental and substance use disorder, the so-called 'dual diagnosis' phenomenon. It represents an unanswered challenge in terms of pathogenic models, treatment and long-term clinical management. Dual diagnosis is a complex and heterogeneous entity and a number of explanatory models of substance use among people with severe mental disorders have been proposed, aiming to test the 'self medication' hypothesis, the potential aetiological role of substance on occurrence of mental disorders, and the common underlying environmental, genetic and biological factors. Furthermore, in the literature attempts have been made to clarify psychopathological characteristics of people who suffer from dual diagnosis. Individuals with dual diagnosis appear to be more often males, with an earlier onset of the mental disorder and more severe clinical and social outcomes. The co-occurrence of mental and substance use disorders complicates treatment, management and prognosis of both disorders, but it remains often unrecognised and undertreated. Mental health and addiction professionals should accurately assess and evaluate this comorbidity, although aetiological links, temporal relationships and psychopathological characteristics are still not entirely clear and, probably, heterogeneous and multifactorial.

Key words

Psychopathology • Dual diagnosis • Comorbidity • Severe mental disorders • Addiction

Introduction

The term *dual diagnosis* has been historically used to define the co-occurrence of mental and substance-related disorders in the same individual. Since the late 1980s, addictive behaviours related to alcohol and illicit substance use have been shown to be highly prevalent in people suffering from severe mental illnesses, such as schizophrenia and major affective disorders [1]. The dual diagnosis phenomenon is a key psychopathological issue, representing an unanswered challenge in terms of pathogenic models, treatment and long-term clinical management. Research in clinical populations with dual diagnosis is consistent in showing poor clinical and social outcomes [2]. Individuals who suffer from both mental illnesses and substance use disorders have an increased likelihood of serious clinical consequences and less favourable long-term outcomes, including, for example, risk of hospitalisation [3], medication noncompliance [4], violence [5], overdose [6] and suicide [7]. The most frequently used substances are tobacco, alcohol, cannabis and cocaine and, especially in the US, rates of substance misuse in people with severe mental illness are considerably higher compared with healthy individuals. According to the *Epidemiological Catchment Area* study [8], about half of people suffering from severe mental disorders have a lifetime comorbid substance use disorder. Moreover, the *National Comorbidity Survey* [9] showed that roughly half of respondents who meet criteria for a lifetime substance use disorder also meet criteria for one or more lifetime mental disorder. Studies in different mental health settings show large differences in dual diagnosis rates among people with severe mental illness, ranging between 20 and 65% [10].

In Europe, moderate size evidence on dual diagnosis has been accumulating since the beginning of the 1990s. Wide variations in rates of addictive behaviours among people with severe mental disorders have been found in European countries [10]. According to the *European Schizophrenia Cohort* (EuroSC) study [11], carried out on 1,208 subjects with schizophrenia in France, Germany and the UK, comorbid alcohol and other psychoactive substances rates were lower than those reported in the US, but higher than the general population. The lifetime prevalence rate for comorbid substance use disorder was 35% in the UK, 21% in Germany and 19% in France.

Despite the high prevalence rates and clinical impact, dual diagnosis and its psychopathological and clinical burden remain often underrated and poorly assessed

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in psychiatric settings. In this overview, we summarise both new and old main issues of dual diagnosis, including psychopathological models, symptoms profiles and clinical issues, aiming to define the peculiar features of individuals with co-occurring mental and substance use disorders.

Psychopathological models and aetiological hypotheses of dual diagnosis

The strength of the epidemiological, clinical and biological association between substance use and severe mental disorders has determined a large number of research initiatives aimed at clarifying the nature of this association. However, there are no clear and uniformly accepted definitions of comorbidity, and dual diagnosis has no coherent theoretical framework [12]. Various conceptualisations of *dual diagnosis* have been suggested to assess if comorbid disorders are part of the same clinical syndrome or represent two or more different and independent conditions [13]. Psychiatric nosology has traditionally emphasised the importance of differentiating temporary psychiatric symptoms observed only in the context of intoxication and withdrawal influences, and psychiatric conditions determining full diagnostic syndromes, independently from the comorbid substance use disorder [14 15]. Although the nosological analysis of comorbidity may enhance the generalisability of research findings [16], dual diagnosis represents a complex and heterogeneous entity, and different drugs and alcohol may not necessarily share identical relationships with different mental disorders. The growing and long-term interest in this area might be considered under several points of views. Under an atheoretical point of view, most research has been focused on the analysis of the correlation between addiction and mental disorders, using disease definitions derived from the standardised diagnostic entities of the DSM and postulating a diagnostic independence of two distinct and comorbid pathological conditions. Nevertheless, it should be highlighted that co-occurrence of mental disorders and addictive behaviours complicates psychopathological features and makes nosology more complex. Clinicians should be aware that reductive categorical or one-dimensional approaches heighten the risk to lose the psychopathological meaning of dual diagnosis phenomenon. Dual diagnosis is not a simple *summa* of two clinical entities to *think*, treat and manage separately, but represent a single pathological entity where different psychopathological elements join together, influencing negatively each other. Indeed, if the focus of categorical diagnoses is addressed to identify elements building categories of subjects who fall into pre-established diagnostic criteria, the diagnostic approach for dual diagnosis should be aimed at recognising those dimensions overcoming diagnostic categories in favour of psychopathology [17]. The interpretation of comorbidity needs a comprehensive awareness that dual diagnosis represents a complex phenomenon in which only a multidimensional understating may allow to fully understand the phenomenon. In such context, it is easy to recognise all problems related to artificial separations of dual disorders, not only in terms of diagnosis and treatment, but also of service organisations [1].

Nevertheless, aiming to build upon a common theoretical framework of dual diagnosis, it may also be useful to analyse etiological models, even if they are incomplete. Indeed, an ideal psychiatric nomenclature needs to define syndromes on the basis of established aetiology and pathophysiology [15]. Theories on potential aetiological links have been widely explored during the last 30 years, but the underlying mechanisms of the association between mental and substance use disorders are not entirely clear. Attempting to overcome the "chicken and egg" paradox [18], a number of explanatory models of substance use among people with severe mental disorders have been proposed. Supporting the paradigm that substance use disorders might be the consequence of mental disorders, the "self medication" hypothesis has been proposed [19]. According to this model, substance use disorder would represent the consequence of a severe mental disorder, occurring in a context of self-regulation vulnerability and individual difficulties in controlling subjective emotions, affects, relationships, and self-care [20 21]. This hypothesis suggests that self-medication by alcohol or illicit substance use may have the role of a coping strategy addressed to treat and reduce anxiety, anhedonia, psychotic symptoms, or painful affect states [20 21]. It has been shown that subjects with mental disorders tend to use substances to relieve depressive symptoms, social withdrawal and apathy. As previously reported, substance use for several patients becomes the instrument that allows to avoid falling into the pain of insight, to make sense of life's experiences, or even moving symptoms that are difficult to express otherwise [17]. Drake & Wallach [22] highlighted that, under a phenomenological perspective, experiences with alcohol and illicit substances represent a confused attempt to survive the stress and other consequences of mental illness, including victimisation, lack of social opportunities and hopelessness. Among people with psychotic disorders, the main reasons for self-medication reported by individuals with alcohol or illicit substances use disorders include relieving depression, achieving or maintaining euphoria, improving self-confidence and social abilities [23]. Data from the *National Epidemiologic Survey on Alcohol and Related Conditions* (NESARC) [24] on 34,653 US adults show that those who had used alcohol

or other psychoactive substances to reduce fear, anxiety, or avoidance symptoms had a significant risk of incident alcohol or substance dependence, with adjusted ORs of 2.6 (1.0-6.7) and 5.0 (1.7-14.2), respectively. However, further findings from NESARC [25] did not support the self-medication hypothesis, highlighting that both mood and anxiety disorders might influence the transition from substance use to abuse and/or dependence rather than from abstinence to use.

It has been suggested that patients may use substances to self-medicate adverse effects of antipsychotic drugs, especially akinesia and akathisia [26 27]. This hypothesis is not totally confirmed by research. Indeed, it has been shown that patients with schizophrenia and comorbid substance use disorder have more extrapyramidal effects than non-abusing patients [28]. For example, cocaine use disorder is associated with severity of dyskinesia, parkinsonism and akathisia [28 29].

Furthermore, the self-medication model should imply that people with mental disorders might have similar patterns in both substance selection and psychopathology, but the available evidence does not entirely support this hypothesis. Self-medication can explain some, but not all, of the reasons for high comorbidity rates among individuals who suffer from mental disorders. Substances used by individuals with mental disorders are widely heterogeneous, with no replicable patterns of abuse/dependence, and appear to be related with other factors in addition to self-treatment. Drug selection appears correlated with environmental factors [30] rather than with specific symptoms of mental disorders, e.g. negative symptoms. No significant differences were found across different diagnostic subgroups on severity, since substances of choice and length and patterns of use seem to reflect those found in the general population [31].

Finally, evidence that people with co-occurring substance use disorder have generally worse clinical features at least partly disproves the hypothesis of self-medication. Substances produce a heterogeneous range of effects, but generally exacerbate rather than relieve symptoms of underlying mental diseases [32]. If alcohol or illicit substances are used to increase pleasure, to *get high* and to reduce negative psychotic and anxiety symptoms, increased depressive or positive symptoms have been reported [33 34]. People with co-occurring severe mental and substance use disorders appear clinically and socially impaired, more severely ill and more often hospitalised or homeless [21]. It is still unclear whether these characteristics are causes or consequences of persistent substance abuse.

The unidirectional causality seems inconsistent and is not totally supported by the temporal relationship between the onset of substance use and the occurrence of mental disorders. It has been highlighted, for example, that alcohol or substance use disorders often precede rather than follow the onset of mental disorders. Hambrecth & Hafner [35] have shown heterogeneous temporal links pointing out that alcohol abuse more often followed first psychotic symptoms, whereas substance abuse preceded psychosis in 27.5%, followed it in 37.9%, and emerged within the same period in 34.6% of the cases. Some reports on the temporal relationship between addiction and mental disorders are also available for anxiety disorders. However, mixed results have been reported and, while social phobia has been predominantly identified as a primary disorder preceding substance use [36], the temporality of other anxiety and substance use disorders is less clear.

The second proposed model involves the hypothesis that mental disorders might be the consequence of a chronic substance use [37]. This widely debated association is essentially based on the stress-vulnerability model in which substance use represents the stressor precipitating the onset of mental disorders in vulnerable individuals [16]. Although some studies have underlined the potential link between alcohol, opioid, stimulant use and the occurrence of different mental disorders [34 38], the association between cannabis use and the development of related psychotic disorders has received particular attention. In the last 20 years, an increasing body of research has explored if cannabis might influence, in a dose-dependent manner, the onset of psychotic disorders. Although findings on cannabis and psychosis association need to be interpreted with caution, there is reasonable evidence from prospective studies that regular cannabis use is associated with an increased likelihood of schizophrenia and other psychotic disorders [39]. Use of cannabis has been suggested to confer about a twofold higher individual risk for later schizophrenia and, at the population level, the elimination of cannabis use might reduce the incidence of schizophrenia by approximately 8% [40].

Systematic reviews analysing the link between cannabis and psychotic disorders added evidence about the potential role of cannabis in the pathogenesis of schizophrenia. Moore et al. reviewed 35 studies on the relationship between cannabis use and the occurrence of psychotic or affective mental health outcomes, and found an increased risk of any psychotic outcome in individuals who had ever used cannabis [41]. Results were consistent with a dose-response effect, with greater risk in people who used cannabis more frequently. Preliminary studies [42] have reported an increasing use of novel psychoactive drugs, such as synthetic cannabinoids, especially among young people suffering from mental disorders. Synthetic cannabinoids may also exacerbate psychotic symptoms in vulnerable individuals [43], and the use of these psychoactive drugs could explain otherwise inexplicable new psychotic symptoms, especially

in young people [44]. It is interesting to note that preliminary data [43] show that the occurrence of psychopathology and symptoms, such as hallucinations, delusions, behavioural problems and loss of control, might be more likely among people using synthetic cannabinoids compared with those using natural cannabis.

The phenomenon of *spiceophrenia* [45] has been recently described exploring relevant research, including surveys, toxicology studies and case series. Although a clear causal association cannot be identified, the available evidence suggests that synthetic cannabinoids may induce acute and transient psychoses in vulnerable people or in individuals with prodromal symptoms as well as relapses in subjects with a history of mental disorders. Symptoms related to acute or chronic use of synthetic cannabinoids highly vary in terms of psychopathology, and seem to be characterised by paranoid thoughts/combativeness/irritability, altered perceptions/mental status, thought disorganisation, confusion, agitation/anxiety/panic attacks/restlessness and depressive states with suicidal thoughts [45].

However, although the aetiological role of cannabinoids in chronic psychosis can be supported by some neurobiological models [46 47], cannabis seems to be neither a sufficient nor a necessary condition for the onset of chronic psychotic disorders, appearing as one of the several known and unknown factors that interact each other increasing the individual risk of psychosis [40 48]. The role of cannabis on psychosis may be a good example of the role of the gene/environment interaction in determining vulnerability in psychiatric disorders [48 49].

Furthermore, the association with cannabis does not appear to be specific. Interestingly, it has been found that cannabis use might play a role also in the occurrence of mental disorders other than psychoses. Preliminary data found that cannabis use might worsen the occurrence of manic symptoms in people with bipolar disorder and might also have an effect on the incidence of manic symptoms [50]. On the other hand, Lev-Ran et al. [51] highlighted that cannabis users have a significantly higher likelihood to develop depression compared with non-users (odds ratio [OR] = 1.17; 95% confidence interval [95% CI]: 1.05-1.30), and this association is stronger among heavy cannabis users (OR = 1.62; 95% CI: 1.21-2.16).

It should be taken into account also the potential role of tobacco that is frequently used in association with cannabis. Rates of smoking among people with psychotic disorders are notoriously high [52], with an estimated prevalence of almost 60% in people with a first episode of psychosis [53]. Even for tobacco, the reasons why people with psychosis are more likely to smoke compared with the general population are still unclear. A recently published meta-analysis [54] reported findings for tobacco similar to cannabis. From prospective studies, an overall relative risk of new psychotic disorders in daily smokers *vs* non-smokers of 2.18 has been found (95% CI: 1.23-3.85). Furthermore, daily smokers developed psychotic illness at an earlier age than non-smokers (weighted mean difference [WMD] = -1.04 years; 95% CI: -1.82 to -0.26). Therefore, the association between smoking and psychosis deserves further examination.

The third model hypothesises that dual diagnosis might be due to shared risk factors common to both mental disorders and addictive behaviours.

Accumulating evidence shows that genetics and gene/environment interaction may represent the common underlying factors between these two disorders [49]. It seems that there may be an overlap between genes identified in schizophrenia and those found in addictive behaviours, i.e., genes involved in neuroplasticity and brain development and genes that modulate the activity of dopamine and other catecholamines [49].

The involvement of brain dopaminergic pathways is likely to be a shared characteristic of dual diagnosis. The mesolimbic dopamine pathway has been implicated not only in the rewarding mechanism implicated in the substance use disorders, but also in the occurrence of positive symptoms in schizophrenia. On the other hand, the mesocortical dopamine pathway is a contributor of the presence of negative symptoms in schizophrenia and has been involved in the neuroadaptation resulting from repeated substance exposures [49].

Recently, a 'cannabinoid hypothesis', other than the 'dopamine hypothesis', has been suggested [55], although findings supporting endocannabinoid system dysfunction in schizophrenia are not entirely consistent across studies. It seems that alterations affecting the cannabinoid CNR1 gene lead to genetic predisposition for schizophrenia [56]. On the other hand, alterations in the endocannabinoid system, such as an increased density of cannabinoid CB1 receptor binding in corticolimbic regions and increased levels of cerebrospinal fluid endocannabinoid anandamide, may contribute to the pathogenesis of schizophrenia [55 56].

Mental and substance use disorders may also share dysfunctional environmental factors, including a disruptive family environment and parental abuse or neglect [57]. Especially among women, a childhood traumatic event might be at least partially responsible for the association between anxiety and alcohol use disorders [58]. Other mediators of the relationship between mental and substance use disorders might be represented by specific personality traits, including sensation-seeking, social anhedonia and impulsivity. In particular, a relatively recent study [59] highlighted that sensation-seeking and social anhedonia are prominent in people with substance use disorders

and schizophrenia, respectively, whereas impulsivity is high in people with comorbid disorders.
Impulsivity, i.e., "a predisposition toward rapid, unplanned reactions to internal or external stimuli regardless of negative consequences" [60] may represent a major common substrate of dual diagnosis. According to the reward-delay or delay discounting model, preference for a small immediate reward over a larger delayed one and an exaggeration of the normal hyperbolic loss in value of a future reward with increased time, characterises vulnerability of people who suffer from both mental and substance use disorders. Impulsivity negatively influences decision making and is frequent in people with alcohol and substance use disorders as well as among individuals who suffer from psychotic, bipolar, stress-related and cluster B personality disorders [7 61 62]. Impulsivity may also be the substrate for the high rates of suicide [7] and violence [63] found in people with dual diagnosis.

Psychopathological features of dual diagnosis

The onset of mental health problems among people with substance use disorders is typically earlier than among those without comorbid addictive behaviours. Meta-analytic data have established the extent to which use of tobacco, cannabis, alcohol and other psychoactive substances affect the age of psychosis onset. It has been highlighted that daily smokers develop psychotic disorders about one year before than non-smokers [52]. Other findings provide evidence for a relationship between cannabis use and earlier onset of psychosis, showing that the onset among cannabis users is about two years earlier than among nonusers [64]. A meta-analytic replication [65] suggests that the association between cannabis use and earlier onset of psychosis is consistent and not influenced by other potentially confounding factors, such as tobacco smoking. On the other hand, alcohol use is not associated with a significantly earlier age at onset of disease [64].
Similar findings have been reported in studies exploring other mental and substance use disorders. For example, the *Sequenced Treatment Alternatives to Relieve Depression* study [66] pointed out an age at onset of the first depressive episode significantly lower among those with comorbid substance use disorder (23.7 vs. 25.7 years).
Furthermore, people with dual diagnosis are more often males. Men with severe mental disorders have higher rates of comorbid substance use than women, while clinical outcomes of both mental and substance use disorders among women might be characterised by poorer prognosis. Although dually diagnosed women have more social contacts and fewer legal problems, they have greater problems with victimisation and medical illness than men [67]. Male patients with dual diagnosis are more likely to be admitted for schizophrenia and to use substances other than alcohol, whereas female patients are more likely to be admitted for affective disorders and to have experienced emotional, physical, or sexual abuse or having been crime victims [68 69].
Individuals with dual diagnosis generally have more severe clinical features than those without comorbid disorders. However, findings are consistently heterogeneous according to type of mental or substance use disorders involved, as well as temporal relationship between psychiatric and addictive disorders [70]. Some research comparing symptoms in people with dual diagnosis with those in non-abusing individuals is available, especially from studies analysing subjects suffering from schizophrenia and other psychotic disorders. Differences between subjects with schizophrenia, using and non-using alcohol or substances, seem not striking, but some interesting symptom patterns have been found [71]. High levels of derealisation, depersonalisation, ambivalence, hopelessness and sudden delusional ideas more often characterise clinical presentations of people with co-occurring schizophrenia and substance use disorder. Psychopathological differences seem mainly related to involved substances, potentially inducing intense hallucinations and psychotic symptoms rather than to a persisting or predisposing clinical pattern. The body of the literature suggests high levels of positive symptoms in dual diagnosis patients than in non-addicted individuals with severe mental disorders.
A meta-analytic comparison [72] based on nine studies (accounting for 725 individuals) tested the hypothesis that people with schizophrenia and comorbid substance use disorder have more positive and less negative symptoms than their non-comorbid counterparts. Although total *Positive and Negative Syndrome Scale* (PANSS) scores did not differ (77.8 ± 14.0 *vs* 79.2±17.0), the meta-analysis highlighted that there were markedly higher PANSS-positive (WMD = 2.01; 95% CI: 1.19 to 2.84), and lower PANSS-negative scores (WMD = -1.86; 95% CI: -2.72 to -1.00) among subjects with comorbid substance use disorders. A similar meta-analysis [73] showed that patients with co-occurring schizophrenia and substance use disorders experience fewer negative symptoms than abstinent individuals. These results suggest either that substance abuse relieves the negative symptoms of schizophrenia or that individuals with fewer negative symptoms would be more prone to substance use disorders. Nevertheless, the available meta-analytic data [74] highlight a small, positive and significant trend for depressive symptoms among dual-diagnosis patients as compared with single-diagnosis individuals, especially for studies using the *Hamilton Depression Rating Scale* to assess symptoms.
Evidence is available also for mental disorders other than schizophrenia. Main differences for dually diag-

nosed individuals with major affective disorders involve higher levels of hypersomnia and anxious mood in people with major depressive disorders [66], and more anxiety and stress-related symptoms in people with bipolar disorders [75].

Symptom patterns of bipolar disorders strictly depend on the substance misused, with cannabis use selectively and strongly preceding and coinciding with mania/hypomania, and alcohol use preceding or coinciding with depressive episodes [76 77].

Moreover, cognitive functioning has been widely explored in people with severe mental disorders. Although use of drugs is associated with impairment in cognitive function in healthy people, the potential role of substance use disorders on cognition of people with mental disorders remains unclear and produces conflicting results, probably related to methodological limitations [78]. It has been shown that some people with comorbid substance use might not have poorer social and cognitive functioning than their non-comorbid counterparts [79]. A matched, cross-sectional study [80] comparing social and cognitive functioning of subjects with psychotic disorders did not find any differences between abusing and non-abusing subjects. A comparative study [81] exploring whether response inhibition and cognitive flexibility are differentially impaired among patients suffering from schizophrenia with or without comorbid substance use disorder highlighted that non-addicted individuals show the most pronounced executive function impairments. A further exploration [82] indicated that schizophrenia is characterised by severe working memory and multi-tasking deficits. However, deficits on performance are not exacerbated by comorbid substance use disorder.

Research on dual diagnosis has highlighted the high risk of subjects with co-occurring disorders in terms of long-term prognosis and treatment response, independently of its specific clinical manifestations. In particular, several studies have reported lower medication compliance in comorbid patients. Severity of symptoms expressed by subjects with dual diagnosis can be due not only to the direct effects of substances on psychiatric symptoms, but also to medication noncompliance [16]. Poor compliance with treatment regimens in comorbid people seems to be associated with more negative subjective or dysphoric responses [83]. It has been reported that patients with dual diagnosis and low treatment compliance are significantly more likely to have comorbid personality disorders, lower global assessment of functioning scores, more medication side effects, lower self-efficacy for drug avoidance and poorer social support than those without treatment compliance problems [84 85]. However, level of insight probably remains the most important factor in determining whether a patient is regularly compliant, after controlling for comorbid substance misuse and other confounding variables [83]. It seems likely that a better understanding of reasons for noncompliance might be helpful in quantifying the amount of noncompliance mediated by severe symptoms and that attributable just to comorbid substance use [16]. Indeed, when comorbid patients are adequately treated for their psychiatric illness, there is a considerable improvement in symptoms, even if substance use remains unchanged [16].

As a cumulative effect of substances, mental disorders and low treatment compliance, people with dual diagnosis have a greater risk to commit suicide. Evidence has shown that people with both mental and substance use disorders have higher rates of both lifetime suicide ideation and suicide attempts. Severity of psychopathology, higher hopelessness and impulsivity, as well as temperament profile, including dysthymic/cyclothymic/anxiety and irritability traits, all may represent important clinical correlates [86]. Co-occurring alcohol and substance use disorders might be related to poor coping skills and social adversities, which are also risk factors for suicidal behaviour[7]. It has been established that the negative effects related to alcohol consumption, bad experiences from drug use, as well as delusions or hallucinations during depressive symptoms, could all represent independent risk factors for suicide attempts in patients with alcohol use disorders and a history of depressive symptoms [87]. Furthermore, impulsivity represents an important feature of people with dual diagnosis potentially complicating course and treatment of both substance use and mental disorders [88 89]. Addiction could play a mediating role on the effect of impulsivity on suicide attempts, fostering aggression and hostility that increase the risk of acting on suicidal thoughts. It is also possible that both suicidal behaviours and alcohol and drug use represent maladaptive strategies to manage negative symptoms and depressive states. Substance use disorders can increase the risk of mood instability – an important factor associated with suicidal thoughts or attempts – among people with bipolar disorders, including the susceptibility to switch from depression to manic, hypomanic, or mixed states [7]. The combination of comorbid disorders, negative environmental effects and a more severe course is consistent with the wide range of factors associated with attempted suicide across a number of severe mental disorders [7].

Moreover, conceptual models hypothesise that individuals with severe mental disorders are at higher risk of committing violent acts, representing itself an established risk factor for violent crimes [90]. However, rigorous research found that the association between severe mental disorders and violent crime is minimal unless the individual is also diagnosed as having a substance use disorder [5]. Meta-analytic data [91] found that the risk of violence is increased in both

individuals with psychosis and substance use disorder (OR = 8.9; 95% CI: 5.4-14.7) than in general population controls, whereas a consistently lower association was found in non-comorbid people with psychoses (OR = 2.1; 95% CI: 1.7-2.7). Furthermore, risk estimates of violence in individuals with psychosis and co-occurring substance use disorders are similar to those in individuals with substance use disorders, but without psychosis. Therefore, psychoses did not appear to add any additional increase to the risk of violence compared with that due to substance use alone [91]. It is possible that psychotic disorders lead to substance use disorders, which in turn increases the risk of violent behaviours, but limited support for this interpretation has been found. An alternative model is that severe mental disorders and violent behaviours co-occur since both are related to common personality traits such as irritability and inadequate coping with anger or stress [5]. Finally, a shared genetic susceptibility to addiction, schizophrenia and violent crime has been suggested.

Violence and serious aggression often precede diagnosis of schizophrenia, even after controlling for preadolescent psychotic symptoms [92 93]. It has been demonstrated that conviction of violence in late adolescence is associated with a fourfold higher risk for a future diagnosis of schizophrenia, suggesting a role of violent behaviour as a part of the prodromal psychosis syndrome. Childhood psychotic symptoms, as well as physical aggression, represent strong risk factors for violence in adults with psychotic disorders [93]. A role of childhood conduct problems has also been hypothesised. Prospective studies have pointed out that childhood conduct problems other than substance abuse represent important predictors of violence in people with schizophrenia [5].

Conclusions

During the past three decades, growing attention has been dedicated to the dual diagnosis phenomenon. The comorbidity between severe mental disorders and alcohol or substance use disorders represents a common and serious clinical challenge, characterised by high prevalence worldwide. The co-occurrence of these disorders complicates treatment, management and prognosis of both disorders, but it remains often unrecognised and undertreated. Mental health and addiction professionals should accurately assess and evaluate this comorbidity, although related aetiological links, temporal relationships and psychopathological issues are still not entirely clear and, probably, heterogeneous and multifactorial. In many countries, the challenges are exacerbated by the mental and addiction disorders being managed in parallel delivery systems staffed by providers with different knowledge base, skills and attitudes. Attempts at integrating service delivery are ongoing, but implementation of common treatment guidelines is not easy.

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