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Serious suicide attempts in outpatients with multiple substance use disorders

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ABSTRACT

Background: Suicide is a major public health concern and suicide attempts (SA) are frequent and burdensome in people suffering from substance use disorders (SUDs). In particular, serious SAs are a preoccupying form of attempt, which remain largely overlooked in these populations, especially regarding basic risk factors such as gender, addictive comorbidity and substance use patterns. Thus, we undertook a gender-specific approach to identify the risk factors for serious SAs in outpatients with multiple SUDs.

Material and methods: 433 Treatment-seeking outpatients were consecutively recruited in specialized care centers and reliably classified as serious, non-serious and non-suicide attempters. We also characterized lifetime exposure to SUDs, including tobacco smoking, with standardized instruments. Current medication, including psychotropic treatments were collected, which informed psychiatric diagnoses. Multinomial regression identified independent factors specifically associated with serious SAs in each gender, separately.

Results: 32% Participants (N = 139, 47% Women and 27% Men) reported lifetime SA. There were 82 serious attempters (59% of attempters), without significant gender difference. Sedative dependence was an independent risk factor for serious SA compared to non-SA in Women and compared to non-serious SA in Men, respectively. Other risk factors included later onset of daily tobacco smoking in Men and history of psychiatric hospitalizations in Women, whose serious SA risk was conversely lower when reporting opiate use disorder or mood disorder, probably because of treatment issues.

Conclusions: Despite several study limitations, we identified subgroups for a better-tailored prevention of serious SAs among individuals with SUDs, notably highlighting the need to better prevent and treat sedative dependence.

1. Introduction

Suicide attempts (SAs) and completed suicide are the most prominent forms of suicide-related outcomes (Geulayov et al., 2016), and suicide is a leading cause of premature death worldwide (World Health Organisation, 2012). Psychiatric disorders, including substance use disorders (SUDs), are very often involved in SAs (Nordstrom et al., 2013; Vento et al., 2011), which are thus strongly associated with the burden and overmortality observed in both opiate and cocaine dependence (Charlson et al., 2016; Walker et al., 2016). For instance, it has been estimated that up to 35% of heroin-related death were attributable to suicide (Darke and Ross, 2002). Preventing SAs is further warranted because they often recur (de Cates and Broome, 2016), such that a past history of SA represents the strongest predictor for future death by suicide (Haw et al., 2007).

In the general population, SAs are overwhelmingly more frequent in

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Women compared to Men (Geulayov et al., 2016). Among psychiatric disorders, mood and alcohol use disorders (AUDs) seem to increase suicidal risk specifically (Poorolajal et al., 2016). Although SUDs represent a strong risk factor for SA, not all individuals suffering from SUDs will ever attempt suicide. In this population, a higher number of comorbid SUDs and other psychiatric disorders, especially major depression, and environmental factors such as unemployment, low educational attainment, divorce and unstable housing have been associated with SAs (van Heeringen and Mann, 2014; Yuodelis-Flores and Ries, 2015). In treatment-seeking individuals, dual diagnosis has been associated with an increase in SA risk, along with – but independently from – female gender and viral hepatitis (Szerman et al., 2012). Furthermore, individuals with SUDs report very high rates of childhood trauma, which have been associated with borderline personality disorder, sedatives dependence and increased SA risk (Daigre et al., 2015). Finally, episodes of increased substance use and/or acute intoxications may also trigger SAs (Artenie et al., 2015; Lejoyeux et al., 2012).

It is noteworthy that completed and attempted suicide have more in common than with suicidal ideation (Courtet et al., 2011; Mullins et al., 2014). Accordingly, medically serious attempts may also represent a distinct population among attempters (Beautrais, 2001; Giner et al., 2014). This suggests that these subgroups should be clearly targeted in research since they exhibit different risk factors and clinical outcomes (Beautrais, 2004). Moreover, assessing a history of SA taken as a whole is subject to recall bias (Eikelenboom et al., 2014). The consensual definition of a serious SA refers either to *actual lethality* (report of medical assistance after the attempt, regardless of the mean that was used) or to *potential lethality* (use of a mean other than superficial cutting or self-intoxication, regardless of further medical assistance) (Levi-Belz and Beautrais, 2016). Yet, to the best our knowledge, this definition has mostly been applied in studies involving general population (Freeman et al., 2017) or psychiatric samples other than SUDs (Beautrais et al., 1996; Olié et al., 2015). Only a couple of studies based on the same cohort have addressed the issue of serious SA in SUDs, namely alcohol (AUD) (Conner et al., 2003) and cannabis (CUD) use disorders (Beautrais et al., 1999). Their main findings were that CUDs interacted with childhood trauma and psychiatric comorbidity in increasing serious SA risk, and that AUDs were rather associated with completed suicide rather than with serious attempts. Serious SAs were overall more frequent in older Men than Women or younger participants, as was evidenced in other samples (Freeman et al., 2017).

Additionally, we and others (Poorolajal et al., 2016; Yuodelis-Flores and Ries, 2015) identified further methodological flaws limiting our understanding of serious suicidal outcomes in SUDs. First, existing data about SAs mainly come from samples with AUDs and opiate use disorders (OpUD), and individuals with different illicit SUDs are usually merged and into a unique subgroup in epidemiological studies (Poorolajal et al., 2016). Second, quantitative variables related to each substance use, such as amounts, ways, or age at onset (AAO) of use, are often absent from previous studies regarding SAs, although they are subject to large variations amongst individuals sharing the same diagnosis of SUD. For instance, in a sample of recent cocaine users attending specialized care setting, the authors reported that age at onset of cocaine use ranged from 11 to 50 years old. The number of days per week using cocaine ranged from one to seven, and that their usual route of intake was snorting for 50%, smoking for 33% and intravenous injection for 17% (Vorspan et al., 2015). Such heterogeneity is likely to affect the risk of SA and their seriousness differentially (Poorolajal et al., 2016). Accordingly, it may be difficult to distinguish the effects of lifetime AUD from those of acute alcohol intoxication (Lejoyeux et al., 2012) in the occurrence of SAs in individuals, who share both. Inhibition deficits, which have been repeatedly found in suicide attempters with affective disorders (Courtet et al., 2011; Richard-Devantoy et al., 2016a) and in individuals with SUDs (Groman and Jentsch, 2012) as well, are very likely to interact differentially with each addictive substance used alone or in combination. Third, data are lacking about associations between tobacco smoking and SA in samples with SUDs, including in recent reviews (Yuodelis-Flores and Ries, 2015) and in studies addressing serious SAs (Beautrais et al., 1999; Conner et al., 2003), despite numerous reports of positive associations in the general population (Poorolajal and Darvishi, 2016) and in clinical samples (Ducasse et al., 2015). Importantly, these associations may not be mediated by other psychiatric disorders (Covey et al., 2012) and are supported by preclinical evidence. They are likely to be multi-directional, such that tobacco smoking may indicate at-risk profiles for SA, aggravate decision-making impairments observed in suicide attempters (Richard-Devantoy et al., 2016b), or represent a proxy marker of more complex addictive, impulsive or anxious clinical profiles. Finally, the impact of gender on serious SAs has only been assessed through multivariate adjustment in existing research, knowing that sample stratification is likely to provide more reliable findings about specific risk factors, which may better inform clinical practice (Culverhouse et al., 2011; Silverstein et al., 2009). To summarize, it appeared warranted to study suicidal outcomes in SUDs on a simultaneously gender-specific and substance-specific basis, with a focus on serious SA, while taking into account the potential effects of comorbid psychiatric disorders and social adversity.

To do so, we recruited treatment-seeking outpatients with multiple SUDs attending tertiary care centers. Our objective was to identify the risk factors for serious SAs with a specific focus on each substance dependence diagnosis and level of use and gender. We hypothesized that (i) serious SAs would be associated with higher levels of addictive comorbidity and (ii) most risk factors and outcomes would be gender-specific.

2. Material and methods

2.1. Sample recruitment

Treatment-seeking outpatients attending tertiary care programs in the Paris area, mostly around 'Gare du Nord' train station, were consecutively recruited through two multicenter study protocols. It is noticeable that, in France, addiction treatment settings are legally bound and organized to remain as accessible as primary care centers to treatment-seeking individuals, even if they are hospital-based. They also warrant anonymity and free access (French Ministry of Health, 2008).

Eligible patients were French-speaking 18+ years old individuals, who sought treatment in any of the participating centers. Further inclusion criteria were:

- Study one (seven sites) = receiving stable methadone treatment for three months or more for treating opiate dependence (see (Mouly et al., 2015) for details on study protocol);
- Study two (six sites) = any past-year cocaine use (see (Vorspan et al., 2015) for details on study protocol);

For the present study, we selected patients fulfilling criteria for either lifetime opiate or cocaine abuse/dependence according to DSM-IV-TR criteria (American Psychiatric Association, 2000). Exclusion criteria were: compulsory treatment or unable to consent for any other reason (non-French speaking, major cognitive impairment). No comorbidity was an exclusion criterion in either study. Both protocols were approved by the local ethics committee: CPP Ile-de-France VI for study one and CPP Ile de France IV for study two (NCT00894452 and NCT01569347, respectively), including for further analysis with the combined sample (CEEI from the Inserm, IRB00003888 in July 2015). All patients received full information by an investigator and provided written informed consent, and study records were real-time monitored and validated by the relevant institutions.