The Addiction to Suicidal Behavior

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Abstract

Addictions have traditionally been restricted to substance use disorders. In the context of behavioral addictions, some individuals could also be addicted to the repetition of suicidal behavior (SB). In 1998, Tullis proposed a theory of suicide addiction, suggesting that individuals addicted to SB might have three characteristics: the presence of childhood trauma, mood disorder, and multiple addictions. In a series of recent studies, we have refined the addictive hypothesis of SB and confirmed that around 10 % of suicide attempters can develop an addiction to SB. In addition to presenting our studies, we briefly review the psychological and neurobiological mechanisms underlying the addiction to SB. Additionally, we suggest that the most evident targets to halt the development of the addiction to SB are the opioid, stress (corticotropin-releasing factor, CRF), and dopaminergic systems.

5.1 Introduction

Addictions have traditionally been restricted to substance use disorders. However, Goodman adapted and merged the DSM-IV criteria of substance dependence with those of pathological gambling (Goodman 1990). Thus, he expanded the focus of addictions by defining a behavioral addiction "as a process whereby a behavior […] is employed in a pattern characterized by loss of control and continuation despite significant negative consequences. It is not the type of behavior, its frequency or its social acceptability that determines whether a behavior pattern qualifies as an addiction […]." His statement preceded a Copernican change that allowed expanding addictions to include behavioral addictions such as shopping, gambling, suntanning, internet use, work, exercise, or even love and sex (Cassin and von Ranson

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2007; Favazza 1989; Goodman 1992; Kourosh et al. 2010; Reynaud et al. 2010; Sanchez-Carbonell et al. 2008; Tantam and Whittaker 1992; Tao et al. 2010). Indeed, behavioral addictions are frequent and share many characteristics with substance addictions (i.e., tolerance, withdrawal, and relapse) (Grant et al. 2006). Substance and behavioral addictions share common neurobiological and genetic underpinnings, and psychosocial factors may account for the variability of expressions of addictions within individuals (Ibanez Cuadrado 2008; Shaffer et al. 2004). In this context, it is surprising to find the paucity of studies testing the hypothesis that some individuals could also be addicted to the repetition of suicidal behavior (SB). The purpose of this chapter is to briefly examine the literature and to offer an explanatory model on the addiction to SB.

5.2 Background

In contrast with the lack of studies addressing a putative addiction to SB, there is substantive literature suggesting that non-suicidal self-injury (NSSI) could be viewed as an addictive behavior (Victor et al. 2012). For instance, Faye suggested that the heightened negative emotional state preceding NSSI is similar to the aversive withdrawal clinical symptoms experienced by drug users (Faye 1995). More recently, Washburn et al. (2010) reported that individuals displaying NSSI often have strong urges to self-injure (Washburn et al. 2010). Furthermore, although literature on this issue is still controversial, some authors have reported that endogenous opioids might be reduced in individuals who engage in NSSI (see Victor et al. 2012 for a review).

As for SB, in 1998, Tullis proposed a theory of suicide addiction (Tullis 1998) that described individuals addicted to SB as having three characteristics: the presence of childhood trauma, mood disorder, and multiple addictions. Until recently, the only study that tested this compelling hypothesis was a report of three cases (Mynatt 2000). One can review the literature on repeated SB that was collected without the influence of Tullis's model to explore whether Tullis's proposed characteristics are related to the repetition of SB or not. Our reading of the literature supports Tullis's hypothesis for two characteristics; both childhood abuse and addictions are associated with repetition of SB (Monnin et al. 2011; Mynatt 2000; Ystgaard et al. 2004). The evidence for mood disorders is, however, more controversial. For instance, Kreitman and Casey (1988) reported that the presence of mood disorders was negatively associated with repetition of SB. Furthermore, one of our studies recently found that both childhood abuse and substance dependence, but not mood disorders, were associated with major repetition of suicide attempts (Blasco-Fontecilla et al. 2014b).

In 2012, we refined Tullis's theory of suicide addiction by proposing that major repetition of SB could also be considered as another behavioral addiction within Goodman's paradigm (Blasco-Fontecilla 2012). Major repeaters (individuals with ≥5 lifetime suicide attempts) represent approximately 10 % of all suicide attempters (Barnes 1986; Bille-Brahe et al. 1996; Kreitman and Casey 1988). These individuals are at higher risk of suicide completion (King et al. 1995; Lewinsohn et al. 1994), are heavy consumers of health resources, and pose a challenge to clinicians (Kreitman

and Casey 1988). We have recently proposed that many of these individuals are addicted to SB (Blasco-Fontecilla et al. 2014b). In the first study comparing with non-major repeaters (<5 suicide attempts), major repeaters were more likely to be female and more likely diagnosed with anorexia nervosa or substance dependence and had higher levels of trait anger with lower levels of anger expression-out. In a second study, we demonstrated that major repeaters provided different reasons than non-major repeaters for the more lethal suicide attempts. Major repeaters significantly more frequently endorsed automatic positive reinforcement ("To feel something, because you felt numb or empty") as an explanation for their SB than the remaining suicide attempters. We found that relieving emptiness may be an important, but not the only, pathway to major repetition of suicide attempts (Blasco-Fontecilla et al. 2015). This is important because, in contrast with other authors who have suggested that NSSI is perpetuated primarily through negative reinforcement (i.e., the removal of negative emotions) (Victor et al. 2012), our findings suggest that major repetition of suicide attempts is perpetuated mainly through positive reinforcement (i.e., the generation of emotions). Finally, in a third study, we explored whether major repeaters are addicted to SB or not using seven criteria: tolerance (Criterion 1), withdrawal (Criterion 2), loss of control (Criterion 3), problems in quitting/cutting down (Criterion 4), much time spent using (Criterion 5), substantial reduction in activities (Criterion 6), and adverse physiological/physical consequences (Criterion 7) (Blasco-Fontecilla et al. 2014a). Total dependence on SB was indicated by the presence of three or more of the seven criteria in the last 12 months. This cross-sectional study at Puerta de Hierro University Hospital (Madrid, Spain) recruited 118 suicide attempters including 8 major repeaters (7 %, 8/118), who were all females. The association between each SB addiction criterion, physiological dependence and total dependence with major repeater status was tested for significance and for effect size with odds ratios (ORs) and their 95 % confidence intervals. As hypothesized, major repeaters met significantly higher frequency of criteria for total dependence on SB, OR = 62.9 (6.4–615). Indeed, 83 % of major repeaters met criteria for dependence on SB. Interestingly, in a similar study focused on NSSI, 98 % of individuals endorsed at least three of the addictive criteria; and 81 % endorsed more than five criteria (Nixon et al. 2002). In our study, a backward stepwise logistic regression model was used to provide an OR between major repeater status and total dependence status corrected by confounding variables (Blasco-Fontecilla et al. 2014a). Age, panic disorder without agoraphobia, borderline personality disorder, history of psychiatric inpatient admission, and total dependence on SB were introduced as independent variables with major repeater status as the dependent variable. The model selected total dependence and age as the remaining significant variables in the last step. Accordingly, we concluded that major repeaters appear to be addicted to SB (Blasco-Fontecilla et al. 2014a).

5.3 Psychological Mechanisms

The cathartic effect of SB (Farberow 1950) and Beck's "sensitizing" hypothesis of SB (Beck 1996) may explain some aspects of the addiction to SB. Beck (1996) suggested that previous SB sensitizes suicidal thoughts and behaviors, such that they

become more autonomous and easily precipitated. Self-aggression ameliorates the physical and emotional tension that precedes SB, depressive and anxiety symptoms, and painful emotions (i.e., hopelessness, emptiness) (Davis 1990; Jallade et al. 2005; Sarfati et al. 2003; van Praag and Plutchik 1985; Walker et al. 2001). In a pilot fMRI study with eight female individuals, mental pain triggering SB was associated with decreased prefrontal activity, whereas "planning and acting out suicidal impulses in response to mental pain" was related to increased activity in the frontal cortex, suggesting that SB reduces mental pain (Reisch et al. 2010). The cathartic effect might be explained by either emotional venting of an unbearable physical and/or emotional state (Jallade et al. 2005; van Praag and Plutchik 1985) or mobilization of interpersonal support (e.g., caring family, medical attention) (Jallade et al. 2005; Walker et al. 2001). Indeed, SB can be used as a signaling strategy within the "bargaining model" of depression, which suggests that SB is a way to impose costs to the social group – family, friends, and colleagues – where there is a conflict (Hagen 2003). In this context, some suicide attempters might raise support from their relatives and, therefore, gain a positive reinforcing effect from SB.

In this regard, Stanley and colleagues suggested that suicide attempters with a history of self-mutilation are a unique subpopulation of suicide attempters who use self-mutilation to deal with mental pain (Stanley et al. 2001). Others suggested that multiple suicide attempters may use self-mutilating behaviors as a way of self-regulating their negative emotions in the short term (Esposito et al. 2003). In the long term, however, self-mutilating behaviors increase negative affectivity and become another stressor (Linehan 1993). Esposito et al. (2003) suggested that suicide attempts may then replace self-mutilation as a way of modulating negative emotions in multiple suicide attempters. In a study comparing 35 suicide ideators and 32 attempters, suicide attempters, relative to suicide ideators, were less likely to display anger after an acute suicidal episode (Negron et al. 1997). Thus, after an initial suicide attempt, suicide repetition may become a coping strategy for dealing with anger, anxiety, and other painful emotions. Beck (1996) suggested that previous SB sensitizes suicidal thoughts and behaviors, such that they become more autonomous and easily precipitated. As suicidal episodes become more easily triggered by stressful life events, they also become more severe and persistent. In other words, repetition of SB may have a sensitization effect. Beck's "sensitizing" hypothesis of SB has gained some empirical support (Bradvik and Berglund 2011; Joiner and Rudd 2000; Joiner et al. 2000). And even after prolonged suicide-free periods, there is the risk of relapse, often precipitated by the same suicide-associated life events, probably in a similar way to that of drug addiction (Hyman 2005).

5.4 Neurobiological Mechanisms

Humans and animals share major neurobiological changes in substance use disorders, including a compromised reward system (dopamine and opioid peptides), overactivated brain stress system (corticotropin-releasing factor, CRF), and

dysregulation of orbitofrontal/prefrontal cortex function and amygdala (Koob 2006; Wise and Koob 2014). All three systems, opioid, dopaminergic, and hypothalamic-pituitary (HPA) axis, interact in the forebrain (Lovallo 2006; Volkow and Wise 2005) and can be activated either by psychoactive drugs or behaviors (Shaffer et al. 2004).

In the light of our previous findings, it is reasonable to hypothesize that the addiction to SB might also involve a compromised functioning of the brain's motivational systems, including the mesocortical dopamine reward system, the endogenous opioid systems (Grigson 2002; Volkow and Wise 2005; Wise and Koob 2014), and an overactivation of the stress system (Lovallo 2006; Wise and Koob 2014). Immediate relief of psychological (mental) pain is probably associated with endogenous opioid release in the central nervous system, as is the case in self-mutilation (Hicks and Hinck 2008). Indeed, in a recent systematic review, the authors suggested that neuropeptides are involved in the pathophysiology of SB (Serafini et al. 2013). The authors concluded that there was an association between SB and some neuropeptides such as CRF, VGF, and neuropeptide Y (NPY), which are key neuromodulators of emotional processing. Moreover, several authors have demonstrated elevated endogenous opioid release following stressful events. For instance, Christie and Chesher (1982) showed that chronic stress in mice produces opioid dependence. Coid et al. (1983) also reported that prolonged mutilating elevates met-enkephalins. This opioid release may ultimately produce tolerance and addiction in vulnerable subjects (Blasco-Fontecilla 2012). In addition, both acute and chronic stress increase the risk of taking drugs (Volkow and Wise 2005), and CRF is involved in the vulnerability of relapse (Sarnyai et al. 2001) and drug withdrawal (Kreek and Koob 1998). CRF is central to both stress and drug withdrawal responses. Indeed, gene polymorphisms of the CRF receptors have been related to exacerbated stress responses and the vulnerability to develop drug addiction (Logrip et al. 2011).

Here, we would like to stress that while dopaminergic and serotonergic dysfunction have been related to SB (Mann and Currier 2007), there is surprisingly little information about the relationship between the endogenous opioid system – i.e., beta-endorphins- and SB. This is somewhat surprising given the role of psychological pain in suicide (Tossani 2012) and the growing evidence linking self-harm and self-injurious behaviors, behaviors closely related to suicide attempts, with the stress and opioid system (Stanley et al. 2010). Indeed, β-endorphin and ACTH, which controls cortisol secretion, are derived from the same precursor, pro-opiomelanocortin (POMC) (Dent et al. 1986; Oquendo et al. 2014). Furthermore, in a recent study of patients displaying repetitive self-injurious behavior (SIB), the authors found that higher probabilities of sequential SIB – in other words, what they called "sequential dependence" to SIB – were associated with lower levels of ACTH measured in the morning or evening (Sandman et al. 2008). Additionaly, there is a strong correlation between the HPA stress system (CRH, ACTH) and beta-endorphins (Traskman-Bendz et al. 1992) (See Fig. 5.1).

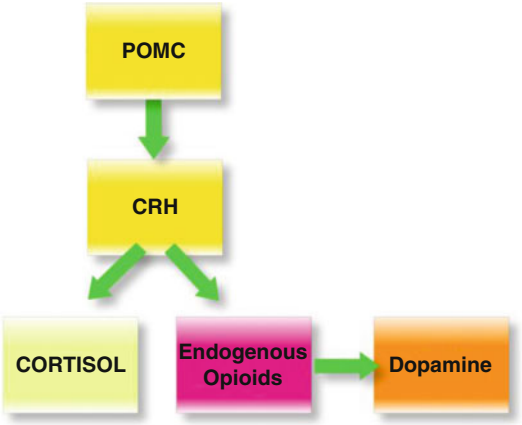

Fig. 5.1 Basic neurobiological mechanisms involved in the addiction to SB

5.5 Significance

There is limited understanding of the factors contributing to suicide attempt repetition and the hypothesis of the addiction to SB offers a plausible explanation for major repetition of SB. This hypothesis may have an important impact in the way we treat suicide attempters characterized by major repetition of attempts. Based on our previous studies, we estimate that around 10 % of suicide attempters become dependent on SB. They are heavy healthcare consumers and pose a challenge for clinicians. If the hypothesis of addiction to SB is further confirmed, this may allow changes in their treatment and help in reducing the associated economic cost associated to the repetition of SB.

As said before, the opioid, dopaminergic, and hypothalamic-pituitary (HPA) axis systems interact in the forebrain. Accordingly, the most evident targets to halt the development of the addiction to SB are the opioid, stress (CRF), and dopaminergic systems. Regarding opioids, yet in 1989, some advocated for clinical trials of opiate antagonists – i.e., naltrexone and buprenorphine – in treating patients with personality disorders and self-injurious behavior (SIB), as they have been found to have elevated levels of plasma beta-endorphin (Konicki and Schulz 1989). Furthermore, the CRF (stress) system has huge potential as a target for pharmacological development (Kreek and Koob 1998). Thus, CRF receptor antagonists, particularly CRF1 antagonists – i.e., antalarmin – show promise for the development of pharmacological treatments for drug abuse and addiction (Logrip et al. 2011). Importantly, CRF1 antagonists could have a lasting effect to blunt the increased stress sensitivity in dependent individuals (Logrip et al. 2011). As for the dopaminergic system, many animal models for SIB share a compromised striatal dopamine system, and the same accounts in several human conditions (Visser et al. 2000). Given that striatal dopamine receptors are coupled to L-type calcium channels, Blake et al. (2007) confirmed their hypothesis that blockers of these channels, such as nifedipine, suppress

SIB in four unrelated animal models (Blake et al. 2007). Unfortunately, 7 years later there is not a single study testing this compelling hypothesis in human beings.

Additionally, given the heterogeneity of SB, other treatments might also be helpful to halt the development of the addiction to SB. Following our model, any treatment alleviating psychological pain might halt the development of the addiction to SB. For instance, lithium, known to have a specific "antisuicidal effect" independently of mood-stabilizing effect (Ahrens and Muller-Oerlinghausen 2001), has an antinociceptive ("anti-psychological pain") action probably mediated through the opioid system (Banafshe et al. 2012). Finally, a recent but promising avenue of research is the use of medications with effects on glutamatergic transmission such as gabapentin, lamotrigine, topiramate, acamprosate, memantine, modafinil, D-cycloserine, and N-acetylcysteine (Olive et al. 2012). As these authors stressed, "substantial evidence has accumulated indicating that ligands acting on glutamatergic transmission are also of potential utility in the treatment of drug addiction, as well as various behavioral addictions such as pathological gambling" (Olive et al. 2012).

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