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The relationship between childhood trauma, early-life stress, and alcohol and drug use, abuse, and addiction: An integrative review

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Abstract
In this review, we discuss the relationship between childhood trauma, early-life stress, and substance use, abuse, and addiction. We further provide theories and neural studies to explain this relationship as well as potential treatment strategies for alcohol and drug abuse and addiction based on understanding types of early-life stressors that lead to both drug use and relapse.

Keywords Stress, trauma · PTSD · Addiction · Types of stress/trauma · Learned helplessness · Neural studies

Introduction

Addiction to drugs is a complex psychiatric disorder that is related to maladaptive and damaging behaviours with devastating consequences for afflicted individuals, their families, and societies at large (Enoch 2011; Goldman et al. 2005; Levran et al. 2012). On a global scale, 4.9% of the adult population suffers from alcohol use disorders, 22.5% smoke tobacco, 3.5% use cannabis and 0.3% inject psychoactive drugs (Gowing et al. 2015). Furthermore, it was estimated that 230 million people around the world have used an illicit drug in 2010 (United Nations Office on Drugs and Crime 2012). The World Health Organisation estimated that there are 185 million illicit drug users worldwide (Goldman et al. 2005).

There have been different reports on the prevalence of childhood trauma among patients with alcohol or drug abuse problems. Grice et al. (1995) reported that over 60% of individuals with drug abuse problems were physically and/or sexually abuse during their childhood. Heroin users were found to experience high rates of childhood trauma such as receiving injuries as a result of physical punishment, penetrative sexual abuse, emotional abuse, and physical neglect. During adulthood, over 25% reported being a victim of unwanted sexual activities and over 27% reported being an adult victim of violence (Shand et al. 2011). As for alcohol, Schwandt et al. (2013) reported that 70% of patients with alcohol dependence have experienced at least one form of trauma in their childhood. Anda et al. (2006) reported that exposure to childhood trauma increase the risk od developing alcohol dependence 7 times than in individuals not exposed to childhood trauma. In addition, Greenfield et al. (2002) also found that childhood trauma is related to relapse in patients with alcohol use disorder, such that 88% of alcoholic patients relapse, while 64% of alcoholic patients without childhood trauma relapse. As for cocaine, Khoury et al. (2010) found that 34% of individuals with cocaine dependence have experienced physical and/or sexual childhood trauma. Gender differences emerged with females more likely to experience a range of childhood traumas which continued after the age of 18 years in the form of unwanted sexual activity and violence.

This review will examine the literature regarding the relationship between early life stress and childhood trauma and alcohol and drug use, abuse, and addiction, and aims to

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highlight the importance of assessing interpersonal early-life trauma and stress factors within clinical settings. This paper will detail animal and human studies that have shown how early life stress and trauma is associated with changes in the stress circuitry of the brain. It will also explore how continuation of addiction and relapse are affected by exposure to stress and its interaction with brain plasticity occurring from addiction (Kreek et al. 2005). The ways in which these phenomena may contribute to developing and/or maintaining an drug abuse and addiction will also be discussed.

Early Life Stress

A stressor is defined as a stimulus that disrupts homeostasis, initiates anticipatory behaviour and physiological responses after repeated exposure, and exceeds the individual's adaptive capacity to return to homeostasis (Burke and Miczek 2014). A stressor may also establish a cycle of distress where the individual learns maladaptive coping strategies and becomes less able to cope with ordinary situations (Tavolacci et al. 2013). Stressors include significant negative life events (e.g., childhood abuse, death of a loved one, parental divorce and conflict), but they may also emerge from daily psychological or social events such as having difficult relationships, living in a disadvantaged neighborhood, and suffering a social stigma (Boardman et al. 2011; Low et al. 2012).

Studies which evaluated individuals with addictive behaviours have found higher levels of self-reported sub-syndromal stress levels compared with controls, which often happened in childhood. These high levels of stress are thought to negatively impact recovery from opioid dependence by increasing cravings and poly-drug use (Jaremko et al. 2015).

Stress responses are essential for survival and are mediated by the hypothalamic pituitary adrenal (HPA) axis, central corticotrophin releasing hormone (CRH) and peripheral catecholamine systems. Chronic activation of the stress response has been shown to increase the risk of psychopathology, including addiction to drugs and alcohol (Enoch 2011).

Rodent studies have found that variations in maternal care in the first two weeks of life are associated with the development of individual differences in HPA axis responses to stress. Maternal licking and grooming in rats mediate the development of central systems that activate or inhibit the expression of behavioural and endocrinal responses to stress. Importantly, these changes to the stress response are passed from mother to daughter, providing a mechanism for individual differences in stress reactivity across generations (Caldji et al. 2003). Hence, early life stress has the capacity to affect neuronal plasticity.

Rodent studies have also demonstrated that early life stress has long lasting effects on the mesolimbic dopamine (DA) pathways (Pêna et al. 2014). Variations within the DA pathways have significant implications for behavioural responses to rewards (Pêna et al. 2014). Enhancement of DA is thought to mediate multiple effects of addictive drugs such as behavioural and motor activation, and the rewarding effects of these drugs. Therefore variations in the DA pathways in rats, is an important finding due to its implication with addictive drugs (Keiflin and Janak 2015).

Microdialysis has been used with animals to show that DA is released in response to stressors such as tail shocks and/or tail pinches. Stress induced DA is released partly by circulating levels of cortisol which itself is increased in response to aversive/stressful events (Pruessner et al. 2004). Pruessner et al. (2004) used positron emission topography with a DA receptor radiotracer to investigate whether early life maternal care could affect lifelong cortisol and DA responses as demonstrated in animal studies. Participants reporting low maternal care had significantly higher overall cortisol responses and higher increase of cortisol during the stress condition, compared to participants with high maternal care. This suggests that early life maternal care may directly alter the dopaminergic and corticosteroid responses to stress in humans as well as rodents (Pruessner et al. 2004). Thus, early life stress can change the structures of the brain which in turn play an important role in addictive behaviors.

HPA Axis

The HPA axis regulates the adrenocorticotropic hormone (ACTH) and cortisol secretion during the stress response. It is vital for cognitive, immune, and behavioural responses to stress (Kuhlman et al. 2015). Cortisol is secreted by the HPA axis under both basal and stress-related contexts,

HPA axis deregulation is defined as the impairment of processes that regulates cortisol production through negative feedback (Hulme 2011). Prolonged exposure to stress can lead to irregular changes in glucocorticoid receptor density. Alternatively, during chronic stress contexts, a positive feedback system may bypass the negative feedback of the HPA axis. This has been demonstrated in animal studies whereby glucocorticoids stimulate the basolateral amygdala, a part of the amygdala that is involved in positive feedback, which in effect, stimulates the HPA axis in a feedforward loop. This is depicted as the stimulation of the basolateral amygdala produces anxiety responses and this feed-forward loop heightens anxiety responses (Hulme 2011).

Interestingly, acute and chronic stress affects the HPA axis and other brain components involved in the stress response, and this may increase the reinforcing effects of drugs during initiation, maintenance, withdrawal, and relapse (Kreek et al. 2005). Addiction has been found to deregulate the HPA axis leading to inability to adaptively and appropriately respond to stress (Zhang et al. 2011). A possible support for this claim can be found in studies which reported heightened cortisol

responses have been documented in recently withdrawn opioid-dependent individuals compared to extended residential treatment care individuals and healthy control groups (Bunce et al. 2015).

Clinical studies with opioid antagonists have shown that the endogenous opioid system also inhibits the HPA axis with the mu receptor tonically inhibiting cotropin-releasing hormone (Levran et al. 2012). Hence it is not surprising that hyporesponsive HPA systems have been identified in cocaine and heroin dependent persons, including individuals receiving methadone maintenance treatment (MMT) (Kreek et al. 2005).

Animal studies have further demonstrated that the chronic administration of drugs has led to molecular alterations in the HPA axis. Rats that were administered a 'binge' of cocaine, for one or two days, presented an increase in plasma corticosterone levels, but these levels weakened after a cocaine 'binge' of 14 days (Zhou et al. 1996). Moreover, it was found that the responses of the HPA axis could be used to assess the likelihood of relapsing in cocaine-dependent individuals (Sinha et al. 2006).

Other studies showed that childhood experience of poor parental care and neglect among cocaine dependent patients, predispose dysfunction of the HPA axis system. The group of abstinent cocaine dependent patients presented significantly higher plasma levels of cortisol, ACTH and prolactine, and significantly lower level of homovanillic than control patients (Gerra et al. 2008).

Childhood Trauma

Numerous studies have demonstrated that childhood maltreatment and early life stressors are associated with increased vulnerability for the development of psychopathology including drug and alcohol abuse (Enoch 2011; Carliner et al. 2016).

Wu et al. (2010) found that most of their substabce abuse patients ($N = 402$) reported exposure to childhood traumatic events. In a study, of the 181 women in a community sample of intravenous drug using, 60.2% were sexually abused, 55.2% were physically abused, 45.9% were emotionally abused, 83.4% were emotionally neglected, and 59.7% were physically neglected. The findings suggest that the prevalence of all five childhood traumas was higher than what has been reported in the general population (Medrano et al. 1999). Heroin users were found to experience high rates of childhood trauma such as receiving injuries from physical punishment, penetrative sexual abuse, emotional abuse, and physical neglect.

Experiencing childhood maltreatment has been shown to impact the severity, course, and duration of alcohol dependence (Lotzin et al. 2016. Treatment-seeking individuals with alcohol dependency who reported exposure to childhood maltreatment, including physical, sexual, and emotional abuse, have been shown to develop alcohol abuse at an earlier age and experience more severe alcohol abuse than patients with no reported exposure to childhood maltreatment (Dom et al. 2007). After controlling for potential confounders (e.g. history of alcoholism in the previous two generations, early-onset alcoholism, or binge-drinking), experiencing two or more adverse childhood events has also been correlated with lifetime alcohol dependence (Pilowsky et al. 2009). Carliner et al. (2016) found that experiencing potentially traumatic events prior to the age of 11 was associated with a higher risk of using marijuana, cocaine, prescription drugs, and engaging in poly-drug use. Furthermore, exposure to interpersonal violent category events (e.g., physical assault, mugging, sexual assault, and kidnapping), were associated with the highest risk of lifetime-use of all drug types (Carliner et al. 2016). This highlights the importance of clinical intervention screening for history of sexual assault victimization in clients who enter psychological treatment for SUD.

Gender differences have emerged between SUD and childhood maltreatment. For example, women who reported experiencing child abuse and neglect were significantly more likely to have used illicit drugs in the past year, compared with men who reported similar childhood traumas (Widom et al. 2006). Childhood maltreatment was found to be significantly associated with alcohol problems for women but not men, and childhood sexual abuse was found to predict substance abuse in women, but not for men (Widom et al. 1995; Widom et al. 2007). In addition, within female sexual assault victims, experiencing interpersonal traumatic events (e.g., stalking, child-abuse, physical abuse, emotional abuse) has shown to relate to using substances as a coping method. However, non-interpersonal traumatic events (e.g., warzones, living in dangerous neighbourhoods, witnessing death) did not have the same association (Ullman et al. 2013). Similarly, emotional abuse and neglect during childhood has emerged as a key predictor for alcoholism, and have been identified as significant contributors to alcohol dependence directly and indirectly, with impulsivity playing a mediating role in the relationship between the two (Schwandt et al. 2013). Furthermore, emotional abuse has been associated with the severity of drug use in treatment seeking patients with alcohol dependence (Dom et al. 2007), and the experience of emotional abuse in conjunction with sexual abuse or emotional neglect can intensify drug abuse problems (Lotzin et al. 2016).

Childhood maltreatment has also been linked with substance abuse during early adulthood. Young adult participants with a childhood history of physical abuse have found to be 48% more likely to use illicit drugs in the past year, and 37% more likely to use illicit drugs in the past 30 days, compared to a non-abusing cohort (Huag et al. 2011). This finding was consistent with those from a study by Thompson et al. (2004) who found that experiencing childhood abuse was significantly related to illicit drug use in the past month. Similar findings for patients seeking treatment for cocaine addiction

reveal that emotional abuse and overall maltreatment during childhood are associated with a younger age of first alcohol and cocaine use, as well as a greater lifetime of severity of substance use (Hyman et al. 2006). Likewise, a strong correlation has been identified between adverse early childhood experiences and an increased likelihood to engage in drinking behaviour during early adolescence (Dube et al. 2006). This connection should be further explored in order to better understand and combat adolescent drinking behavior.

Higher levels of childhood emotional abuse and neglect was higher in a substance-abusing inmate population, as well as higher levels of impulsivity, hostility and suicide ideation in comparison to non-substance abusing inmates (Cuomo et al. 2008). Additionally, substance-dependent inmates also reported more violent behaviours during detention, more juvenile convictions, higher levels of neuroticism. Psychoticism, and impulsivity, and decreased resilience (Cuomo et al. 2008).

Higher levels of childhood maltreatment have been shown to correspond with poorer treatment outcomes for patients with drug related disorders. Higher severity and frequency of childhood trauma is related to higher levels of personality disorder symptoms and an earlier onset of substance use for drug abuse patients (Ruggiero et al. 1999). Increased severity of childhood trauma was found to be related to more severe psychiatric symptoms and more risky behaviour (e.g., unprotected sex) in patients with drug related disorders compared to those with lower levels of childhood trauma (Ruggiero et al. 1999). In regard to treatment efficacy, alcohol dependent patients who reported experiencing childhood trauma benefited less from treatment, and were abstinent for shorter periods of time (Evren et al. 2009; Greenfield et al. 2002; Lotzin et al. 2016; Walitzer and Dearing 2006). These results are important for substance abuse treatment interventions as such interpersonal trauma factors may increase the risk of developing and maintaining substance use disorder, as well as heighten the risk of relapse.

Conclusion

In summary, strong evidence exists that experiencing interpersonal childhood trauma is linked to an increased vulnerability for SUD (Enoch 2011; Lotzin et al. 2016; Pilowsky et al. 2009; Schwandt et al. 2013). This may be influenced by the permanent changes that early life stressors do to the brain's stress circuitry (Enoch 2011).

Evidence also exists that acute and chronic stress affects the HPA axis and this increases the reinforcing effects of drugs (Kreek et al. 2005). Stress is also thought to enhance all stages of drug use, from initiation through to dependence, and relapse (Kreek et al. 2005). Overall, the findings entailed in the present review highlight the need for a multidimensional approach to strengthen substance abuse recovery interventions within clinical environments (Bunce et al. 2015).

Compliance with Ethical Standards

Disclosure of Potential Conflicts of Interest The authors have not received any funds related to this study and do not have any conflict of interest.

Research Involving Human Participants and/or Animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent No informed consent was obtained in the study as it did not involve human participants.

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