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Explicating the role of empathic processes in substance use disorders: a conceptual framework and research agenda

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Abstract

Issues—Elucidating the role of empathic processes in developmental pathways to substance use disorders could have important implications for prevention.

Approach—We searched the biomedical and social sciences literature to determine what is known about empathy and psychopathological manifestations of severe lack of empathy in the initiation, development and maintenance of psychoactive substance use. Thirty-seven empirical studies were identified and formally reviewed.

Key Findings—Adults with alcohol and stimulant use disorders exhibited detectable impairments in both cognitive and affective empathy, measured behaviourally, neuroanatomically, and by self-report, relative to controls. There were no developmental studies specifically designed to test the role of empathy in substance use pathways, but several studies that included measures of empathy suggest that empathy may be protective. Studies on severe empathic deficits were mixed regarding a unique role of empathy in substance use trajectories, independent of interpersonal style, impulsivity and social deviance.

Implications & Conclusions—In the context of findings and methodologic limitations of this review, we recommend more rigorous examination of empathy across the spectrum of substance use behaviour. Future work should utilise: (i) prospective assessment of empathic capacity in substance abusers during and following treatment; (ii) large, developmentally-based prospective designs beginning prior to substance initiation incorporating multiple measures of empathy; (iii) assessment of the moderating role of gender, race, and ethnicity; and (iv) prospective study of empathy in children at elevated risk for substance use disorders.

Keywords

empathy; theory of mind; callous-unemotional; psychopathy; substance abuse

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1. Introduction

Among all individuals who initiate addictive substance use, some go on to develop a substance use disorder, but most actually do not [1]. Social impairment, which constitutes one of four diagnostic domains that characterise substance use disorders [2], includes the failure to fulfil major role obligations, the recurrence of social or interpersonal problems, and giving up important social activities due to substance use. Thus, those who transition from initial non-pathologic use to disordered use often increasingly give up social interactions and obligations in favour of obtaining, using and recovering from substance use. Premorbid functional impairment in other substance use disorder diagnostic domains besides social impairment—namely, impaired control, risky use and pharmacologic changes—have been investigated as intermediate phenotypes that increase vulnerability for addiction. For example, regarding the domain of impaired control, poor impulse control and disruptive behaviour in childhood increases vulnerability to substance use and abuse in adolescence [3,4]. With respect to the risky use domain, novelty seeking and risk-taking in adolescence are established risk factors for substance abuse [5,6]. Finally, with respect to pharmacologic changes, pharmacogenetic differences in alcohol metabolism that account for differences in the development of tolerance and withdrawal are thought to contribute to the large inter-individual and inter-population variations observed in the prevalence of alcohol use disorders worldwide [7].

In contrast, less is known about whether premorbid impairments in social functioning renders some individuals more vulnerable to addiction than others. Rather, impairments in social functioning associated with substance use disorders are generally conceptualised as consequences *resulting* from substance use, mediated by the greater salience provided by substances of abuse relative to day-to-day social activities [8]. In essence, social activities may no longer ‘compete’ effectively with addictive substances in the brain of an addicted individual [9]. What is *not* known is whether individuals who find social interactions less rewarding or salient to begin with are more likely to initiate substance use or transition from experimental to problematic substance use because social sanctions are less salient to them relative to their peers, who derive greater reward from social interactions.

We have previously proposed that empathic capacity may influence substance use behaviour during pregnancy. Women who report feeling more emotionally attached to the fetus during pregnancy are significantly more likely to quit smoking by the third trimester [10]. Pregnant women who abstain from alcohol, tobacco and illicit drugs report greater adequacy as a provider for others [11]. In fact, a greater capacity to recognise facial expressions of sadness, anger and fear in others has been independently associated with a lower likelihood of smoking during pregnancy for women with a genetic predisposition to sensitivity to social context [12]. Extending this framework, we propose the examination of empathy in relation to substance use during other times in life.

1.1 Empathy: definitions and related constructs

In this paper, we define empathy broadly, as a multi-faceted construct that includes a *cognitive* component—the ability to understand the perspective of another via an accurate

perception of social and affective cues—and an *affective* component that includes the ability to experience the feelings of another (sometimes termed *affective sharing* or *emotional empathy*), and also the capacity to care about their well-being (sometimes called *empathic concern*) [13]. Empathy varies along a spectrum; rather than having empathy or not having empathy, literature supports a wide range of inter-individual variation in empathic capacity overall, and also variation in specific components of empathy [14]. The terms, *empathy*, *empathic processes*, *empathic capacity* and *empathic ability* will be used herein to refer to the interplay of these cognitive and affective components.

In normal development, some capacity for empathy can be observed in toddlers, who exhibit prosocial helping responses to others' distress [15]. Empathic ability requires not only the ability to experience another's emotion, which can occur automatically, but also a self-other awareness that distinguishes empathic concern (caring for another) from emotional contagion (simply feeling distressed because someone else is distressed) [16]. A related concept, *theory of mind*, refers to the ability to attribute mental states to oneself and others and to understand that others have beliefs, desires, intentions, and perspectives that are different from one's own [17,18]. The capacity for emotional regulation may be construed as a necessary component of empathic behaviour—adequate regulation of one's own emotions allows for responding with other-oriented empathic concern, rather than responding in a self-oriented fashion so as to relieve personal distress associated with emotional contagion [19]. Finally, there have been substantial efforts to identify neural substrates of empathy and its components—cognitive and affective components of empathy appear to correlate to specific regions including, but not limited to, the prefrontal cortex, insula, limbic system, and frontoparietal networks that subserve self-awareness, mental flexibility, and emotional regulation [20].

1.2 Empathic behaviour appears to be reinforcing

Specifically relevant to addictive behaviour, motivation to care for others appears to be associated with positive feelings, which seem to reinforce empathic behaviour, and the overlap between affiliative and drug-taking behaviour has been previously described [21]. Behavioural and functional neuroimaging studies indicate that kind acts may enhance personal well-being via the release of dopamine through the projection of neural pathways from the brainstem to the nucleus accumbens [22]. Empathic processes may also attenuate stress—empathic concern has been shown to reduce cortisol activity in response to stressful situations among participants who gave social support to a partner during an experiment [23]. Empathic concern has also been associated with activation of reward centres in the ventral striatum and ventromedial prefrontal cortex among mothers who were asked to make caregiving decisions to meet the needs of their children [24]. In summary, empathic processes, and in particular, empathic concern, could have a powerful influence on reward and behaviour [25].

1.3 Disorders characterised by impairment in some components of empathy are associated with a higher prevalence of substance use disorders

Deficits in one or more components in empathic processing have been identified in a number of major neuropsychiatric disorders in which substance use disorders are over-represented.

Cognitive empathy impairment is common in schizophrenia [26], bipolar disorder [27,28] and borderline personality disorder [29]. These deficits are thought to partially account for observed impairments in social functioning among individuals with these disorders [30–32]. In conduct disorder and antisocial personality disorder, characterised by a pervasive pattern of disregard for or violation of the rights of others [2], decrements in empathic concern are thought to underlie the severe antisocial pathway, characterised by callousness and psychopathy [33]. Impairments in processing of others' distress cues, particularly of fear, have been identified in individuals with a pattern of callous behaviour, beginning as early as the preschool years [34,35]. Yet, while individuals with schizophrenia, bipolar disorder, borderline personality disorder, and callous/antisocial syndromes show increased rates of substance use disorders relative to individuals without these disorders [36], the role of empathy, or a severe lack of empathy, as an independent risk factor for substance use disorders has not been specifically examined to our knowledge.

1.4 Could empathic capacity critically influence substance use trajectories?

According to problem behaviour theory [37], children with a severe deficit in affective empathy, or callous-unemotional (CU) traits, may be at increased risk for early substance use due to their response, or lack thereof, to social morays. Specifically, children with CU traits appear relatively insensitive to punishment and social disapproval, rendering them prone to risky or prohibited behaviour regardless of negative consequences or responses from others [33]. Yet, while links between psychopathy and substance use in adolescence have been demonstrated [38–40], whether the specific component of psychopathy relating to lack of empathic concern confers a unique risk for substance use disorders is unclear.

Also unclear is whether high empathic capacity could confer a protective effect. In Figure 1, we illustrate a hypothesized (and simplified) schematic of how a spectrum of empathic capacity might positively (right) or negatively (left) influence the progression from initial substance use to repeated or casual use, from casual use to problematic use, and from problematic use to addiction. Certainly, increased risk-taking is characteristic in adolescence, mediated by more prominent development of reward systems relative to executive control circuits [41]. However, individuals high in empathy, who highly value social rewards, might be relatively protected from making the critical transitions to increasingly problematic use, as shown. For example, if a loved one expresses concern, anger, or fear in response to an individual's initial or casual use of an addictive substance, highly empathic individuals might be more strongly deterred from continuing, so as not to cause further distress in their loved one. Importantly, for criticism or punishment to serve as a deterrent, both cognitive empathy (the accurate perception of others' distress) and affective empathy (caring about their distress) are hypothesized to be important. In particular, those with a severe lack of empathic concern, or callousness, may even fail to recognise cues of fear expressed by others [35]. Thus, we hypothesize that impairment in empathy, in particular affective empathy, could render individuals less sensitive to environmental cues that dissuade escalation of use, enabling a progression towards addiction.

1.5 Why study empathy and substance use disorders?

While many risk factors for substance use disorders are difficult if not impossible to change (male gender, family history of addiction, having another mental health condition), some components of empathy may be modifiable. Brief interventions have been shown to improve empathy in diverse populations including romantic partners [42], in health care providers [43], in child welfare workers [44], and even in male parolees [45] and prison inmates [46]. Furthermore, brief training interventions aimed at increasing parents' empathy towards their children are effective in reducing harmful parenting practices and can improve relationships between parents and their children [47–51]. If empathy is protective against developing substance use disorders, empathy training interventions in children at elevated risk for addiction could represent a novel preventive approach.

Empathy also appears to be temporarily modifiable following intranasal oxytocin administration in healthy subjects and in adults with disorders characterised by impairments in empathy (see Bakermans-Kranenburg and van Ijzendoorn, 2013 [52] for a review and meta-analysis). Individual differences in the oxytocin system that subserves empathic processing have been shown to influence the effects of drugs and alcohol via interactions with several neurotransmitter systems, the autonomic nervous system, and the hypothalamic pituitary-adrenal-axis [53]. In summary, if empathy does influence substance use trajectories, interventions that support the development of empathy in at-risk youth could represent a powerful preventive strategy, while the development of novel pharmacologic agents involving oxytocin could be promising. For these reasons, we attempted to integrate broad fields of research to answer the following questions:

1. Do individuals with substance use disorders have impairments in empathy?
2. What is known about the relationship between empathy and severe decrements in empathy in the initiation, development, and maintenance of substance use?

2. Material and methods

2.1 Search strategy

To search the biomedical and behavioural literature, we used Scopus® (Elsevier) and PsycINFO® (EBSCOhost). Scopus is the world's largest online bibliographic database of peer-reviewed academic journals in the life sciences, physical sciences, health sciences, and social sciences and humanities from 1960 to the present and includes within it all MEDLINE and Embase citations. We conducted two separate searches in Scopus as described in detail in Figure 2; first, on empathy and related constructs (theory of mind and social cognition), and then on disorders characterized by severe deficits in the affective component of empathy (CU traits, psychopathy and psychopathic traits). We then conducted a similar search using PsycINFO. Articles were limited to empirical papers published in English in peer-reviewed journals that contained direct measurements of affective empathy, cognitive empathy (including theory of mind), or manifestations of lack of affective empathy, isolated from commonly co-occurring traits, as described below.

2.2 Selection of articles

CU traits, for the purposes of this paper, were construed as a proxy for a severe lack of affective empathy; CU traits are often measured and linked, perhaps phenotypically, to conduct problems [54]. Thus, the first inclusion criteria was the assessment of CU traits independent of conduct problems. Next, psychopathy, like empathy, is multifaceted, and includes as key features: (i) impulsivity; (ii) failure to adopt interpersonal conventions of honesty, modesty and trustworthiness; (iii) failure to experience genuine emotions regarding others (e.g. love, empathy, guilt); (iv) failure to adopt prevailing sociocultural norms pertaining to financial responsibility and safe conduct; and (v) failure to obey the laws of a given society [55,56]. Importantly, individuals with psychopathy may be normative or high in cognitive empathy, yet low in affective empathy, in particular, empathic concern [57] — this combination could facilitate characteristic interpersonal exploitation observed in psychopathic individuals [58]. While there is some debate over the factor structure of psychopathy, with two, three, four and even five factor models having been proposed, two factor models (interpersonal/affective and social deviance/risk taking) and four factor models (interpersonal, affective, risk-taking and social deviance) are most commonly used [55,59]. To most precisely examine lack of affective empathy alone, we included studies that either isolated the affective facet of psychopathy, or examined a combined interpersonal/affective facet, separate from impulsivity, risk taking and social deviance components.

3. Results

Thirty-seven articles meeting criteria (Figure 2) were identified and formally reviewed. The bulk of literature resulting from the empathy search concerned empathy among providers — these were excluded. Nineteen empirical articles that compared empathy in substance abusers relative to controls are shown in Table 1 in alphabetical order by first author. Four studies that examined the relationship between empathy and various substance-related behaviours are listed in Table 2. Fourteen articles were identified that specifically examined either callous-unemotional trait, the interpersonal/affective factor of psychopathy (using a two factor solution), or the affective facet of psychopathy alone (using a four factor solution), and substance use or substance related behaviour (Table 3). Sample characteristics, study design, measures used to assess empathy or deficits in empathy, analytic approach including covariates, findings, and limitations of all formally reviewed studies are listed in Tables 1 – 3.

3.1 Empathy in individuals with substance use disorders versus controls

3.1.1 Empathy assessed using behavioural measures—Compared to controls, individuals with alcohol dependence exhibited impairments in recognizing facial and eye expressions of emotion across the spectrum of valence (sadness, happiness, disgust, anger, fear) [60–63]. Use of an interview to assess theory of mind showed similar results, and the severity of deficits in alcoholics was unrelated to how many years individuals had abused alcohol, which ranged from 3 to 40 years [64]. Alcohol-dependence-related impairment in theory of mind was shown to be limited to insular dysfunction in one functional magnetic resonance imaging study that compared individuals with schizophrenia alone, schizophrenia and alcohol dependence, and alcohol dependence alone [65]. Reduced emotional contagion

was detected in alcoholics relative to controls [66]—moreover, individuals with early onset alcoholism (Type II) mimicked anger more intensely relative to other presented emotions—this bias was not observed for Type I alcoholics or controls. Cocaine users showed impairments in affective empathy [67], and impairments in more complex social cognitive abilities when viewing multiple verbal and non-verbal cues [68]. In methamphetamine abusers, deficits in theory of mind, recognition of fearful faces, impairment in empathic concern, and hypoactivation in neuroanatomical areas thought to subserve empathic processing were found [69–71].

3.1.2 Empathy assessed using self-report only—Four studies using a range of empathy questionnaires in varied populations all showed that alcohol or drug-dependent individuals reported lower empathy relative to control participants [72–76]. For example, weight-lifters using anabolic steroids reported lower empathy relative to weight-lifters who did not use steroids [77]. In contrast, Bucher et al. (2013) [78] found no difference in empathy between medical students who reported abusing stimulants and medical students who did not.

3.2 Empathy or deficits in empathy and substance use behaviour

3.2.1 Longitudinal Studies

3.2.1.1 Non-referred samples: One study involved a non-referred sample of 521 boys and girls who had self-and parent-reported CU traits assessed in the 6th grade followed by self-reported substance use assessed in the 9th grade [79]. While adolescent-reported CU traits were unrelated to substance use outcomes, parent-reported traits did predict a greater likelihood of onset of substance use (alcohol or marijuana), recurrence of use, and use-related impairment by the 9th grade, independent of their level of conduct disorder symptoms. Hyde and colleagues (2015) [80] showed that self-reported CU traits in 268 low-income 17-year-old boys predicted a substance dependence diagnosis at age 20. Again, this was true even when accounting for conduct symptoms (rule-breaking and aggression) [81]. In contrast, Colins and colleagues [82] did not find a predictive relationship between affective and interpersonal dimensions of psychopathy and later self-reported excessive alcohol or marijuana use.

3.2.1.2 Clinical samples: Hemphala and colleagues' study of 145 adolescent boys and girls who had contacted a substance abuse treatment program did not show any unique effect of the affective facet on substance use outcomes [83] while Swogger and colleagues (2016) [84] showed that the affective facet uniquely predicted fewer days abstinent and less benefit from a brief motivational interviewing intervention.

3.2.1.3 Incarcerated samples: One longitudinal study of 1170 male felony offenders aged 14 – 18 years old showed that CU traits predicted frequency of substances use five years later, above and beyond peer deviance, school dropout, neighbourhood conditions, single-parent household, family arrests, intelligence, executive control and anxiety [85].

3.2.2 Cross-sectional studies

3.2.2.1 Non-referred samples: Six studies examined the cross-sectional relationship between empathy ($n = 2$) or deficits in empathy ($n = 4$) and substance use behaviour in non-referred samples. Beginning with studies of adolescents, Nguyen and colleagues (2011) [86] demonstrated that empathy in 498 African American adolescents was positively correlated with reported drug refusal efficacy and negatively correlated with reported past-30-day drug use. Moreover, drug refusal efficacy mediated the link between empathy and lower drug use. In 776 Dutch adolescents, callous-unemotional traits were associated with positive screens for drug and alcohol use disorders in boys, and alcohol use disorders in girls [87]. A small survey study of 52 self-identified drug-using adolescents revealed no relationship between empathy and drug use behaviour [88].

In adults, Neumann and colleagues showed a correlation between empathic deficits and alcohol use in a non-referred sample of white men, but not in women or in African Americans in a racially diverse sample of 196 men and 318 women [89]. Finally, in a single study of empathy and substance use in pregnant women, Massey and colleagues (2015b) [12] showed that, among women with genetic variants of the oxytocin receptor gene (*OXTR*) previously linked to increased sensitivity to social context [52], heavier smoking during pregnancy was related to impairments in cognitive empathy—specifically, the recognition of sadness, anger and fear in others.

3.2.2.2 Treatment and incarcerated samples: McCown [90] showed that higher empathy in 97 Twelve Step group attendees was associated with reports of spending more time involved in recovery activities, more time abstinent, and more time engaging in self-help activities in general over their lifetimes. However, groups included Al Anon and Narc Anon—these participants may not have had substance use disorders and the proportion of respondents constituting these groups relative to others was not reported.

Cross-sectional studies of psychopathic traits and substance outcomes in incarcerated samples were the most mixed; studies by Gustavson (2007), Walsh (2007), Durbeej (2014), Patrick (2005), and Reardon (2002) all measured the affective facet of psychopathy separate from the interpersonal facet and showed mixed findings [91–95]. Durbeej et al. (2014) [93] showed that lack of affective empathy was associated with poorer participation in substance abuse treatment and dry housing. Studies by Patrick et al. and Reardon et al. suggested no relationship between deficient affective empathy and smoking or alcohol problems, respectively, among male prison inmates [94,95]. Walsh demonstrated that empathic deficits were associated with younger age of onset of substance abuse, and the prevalence of substance use disorders, respectively [92], while Schulz et al. showed that the combined affective/interpersonal facet of psychopathy was associated with a *later* age of onset of drug use, though only among women [96]. Finally, among male inmates, callous interpersonal style was directly related to substance use symptoms, while deficient affect was inversely related [92].

4. Discussion

We attempted to comprehensively review and integrate findings from diverse fields of research to examine the potential importance of empathy, and severe deficits in empathy, in substance related behaviour across the diagnostic spectrum of substance use. It is important not to confuse this synthesis of research with a formal systematic review – our approach, while quite extensive, may not be exhaustive. Moreover our hypothesized model of the role of empathy (Figure 1) may constitute one of many components in a complex pathway. For example, early impulsivity associated with callousness, psychopathy or depression could adversely influence the *development* of empathy, thereby increasing risk for progression towards addiction [97]. Moreover, while most commonly conceptualised as a trait, empathy may fluctuate as a function of the immediate social context [98].

Within these limitations, it is clear from research to date that adults with a variety of substance use disorders demonstrate impairments in various facets of empathic processing compared to healthy controls. Whether these differences reflect the acute or residual effects of intoxication and/or withdrawal, or individual differences that predate substance use cannot be determined based on these studies. The relatively few longitudinal studies that assessed empathy prospectively, as it relates to substance use outcomes, do suggest its potential importance, while studies focused on a severe lack of empathy are mixed regarding any unique role of empathy. To further explicate this question, we propose several directions for future research. Of note, alexithymia, which refers to difficulty recognising, processing and regulating emotions in *oneself*, though not necessarily others, has similarly been observed in individuals with alcohol use disorders, though its role as a risk factor for alcohol use disorder has not been established [99].

4.1 Research on substance abuse treatment outcomes should examine empathic capacity prospectively

Given the importance of empathic ability in optimal social functioning [100], understanding whether empathic impairments improve with treatment is important to achieve the best short- and long-term substance abuse treatment outcomes. Empathic deficits could affect the ability to engage fully or adaptively in treatment groups and sober-living residences [93], and ongoing difficulties with empathic processing could influence the quality of social relationships even when abstinence is achieved and maintained. Difficulties in psychosocial functioning could heighten the risk for relapse via a number of mechanisms including stress [101] and social isolation [102]. For example, the bias toward expressions of anger observed among Type II alcoholics [66] could adversely influence interpersonal relationships with treatment providers and other important individuals who may be in the role of supporting their recovery.

Another understudied, yet potentially relevant area of research concerns the role of empathy in recovery from addiction in the context of Twelve Step activities [90]. The treatment of addiction is often conducted outside conventional medical and psychiatric settings in the separate ‘addiction treatment community’ [103]. Perhaps related to this separation, while Twelve-Step recovery groups are viewed as a mainstay of treatment for many providers and recovering individuals alike, there is surprisingly little formal investigation into the neural

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underpinnings of the Twelve-Step recovery process. It is known that other-oriented interest, related to empathy, appears to increase with Alcoholics Anonymous participation over time [104]. Moreover, it has recently been suggested that increased empathy, theory of mind, affective sharing, and reconstruction of autobiographical memory through Twelve-Step activities could mediate the beneficial effect of Twelve-Step activities on maintaining abstinence for attendees [105]. Indeed, memory appears to be closely integrated with theory of mind ability in healthy individuals [18]; application of these and other recent advances in social and cognitive neuroscience [106] to the study of how Twelve-Step activities effect personal change in its members yields the possibility of elucidating the neural underpinnings of this enduring recovery approach. This knowledge then, can directly inform a general understanding of how abstinence from psychoactive substances can be successfully maintained over time.

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4.2 Developmental studies of pathways to substance use disorders should include multi-method assessments of empathy, beginning prior to the onset of substance use

While we have clues that empathic processes could play an important role in the onset and maintenance of substance use, much more work is needed. Empathy was related to drug refusal efficacy among 6th grade children, but this was studied cross-sectionally [86]. One single longitudinal study has assessed CU traits prior to the onset of use [79]. Here, self-reported CU traits showed no relation to later initiation of substance use, but *parent-reported* traits did, and did so independent of conduct symptoms. Yet, three of the four items used to assess CU traits in this study could reasonably represent proxy measures of deficient empathy, namely, lack of remorse/guilt, callousness/lack of empathy, and shallow/deficient affect. The ‘unconcerned about school performance’ item may be more of a measure of social deviance than lack of empathy. This limitation also applies to the Hyde study (2015) [80] showing that CU traits in low-income boys’ predicted a substance dependence diagnosis three years later. Thus, even with conduct symptoms controlled in these last two studies, the CU subscale cannot be interpreted as the exact opposite of affective empathy.

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Similarly, the affective facet derived from the Hare Psychopathy Checklist-Youth Version includes the failure to accept responsibility, along with lack of remorse, shallow affect, and lack of empathy. Accepting responsibility could be construed as a feature of prosociality, which is related to, but not equivalent, to empathy—those who are empathic tend to exhibit prosocial behaviours [107], but prosocial behaviour can exist in the absence of empathy [108]. Thus, while four longitudinal studies showed that traits associated with deficits in empathy predicted more severe substance use outcomes [79,80,84,85], the direct measurement of empathy prior to the onset of substance use is critical to examine whether high empathy could be protective. As above, examining how traits such as impulsivity could hamper the development of empathy is also warranted [97].

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4.3 Studies of empathy and substance use outcomes should consider the effects of gender, race, and ethnicity

Conflicting findings among studies could have reflected the moderating effect of gender in substance use disorder trajectories [109]. For example, among boys in the Wymbs study (2012) [79], those with high CU traits were most likely to report recurrent marijuana use,

alcohol use and impairment due to use. However, in girls, those who reported low CU traits and high conduct disorder symptoms were the most likely to endorse onset, recurrence, and impairment due to alcohol, as well as recurrent and impairing marijuana use. Could CU traits actually be relatively protective in girls? Interestingly, Schulz et al. [96] also found that the interpersonal/affective dimension of psychopathy appeared to be protective in women – it was associated with a later onset of drug use. Future studies should investigate gender differences in the influence of empathy or empathic deficits on substance use behaviour.

The relationship between empathy and substance use outcomes could also differ by race, as suggested by Neumann's (2008) [89] findings of a link between the affective dimension of psychopathy and alcohol use in white men, but not in women, or in African Americans. Indeed the potentially confounding role of race in the relationship between empathy and substance use disorders is likely complex for several reasons. First, racial differences in both the prevalence and correlates of substance use disorders have been documented in community samples [110] and in criminal justice populations [111]. Next, while the psychometric properties of Hare Psychopathy Checklist-Revised (PCL-R) total scores appear to be similar for African American and European American offender populations [112], African-American inmates characterized as psychopathic using the PCL-R do not demonstrate the same emotional processing deficits observed in white psychopathic inmates [113]. This raises the possibility that the PCL-R does not measure the same latent construct across races. More broadly, the nature of the relationship between psychopathy and race remains controversial [114,115]. In summary, future work to elucidate a potential role of empathy and empathic deficits on substance use disorder outcomes should carefully consider the role of gender and race in study designs.

4.4 Identification of protective factors in children at risk for substance use disorders is needed

Confirming a protective role of empathy in the development of substance use disorders yields the power to intervene early, particularly in children at increased risk for substance use disorders [116]. Unfortunately, there is little research to date on preventive interventions developed around protective factors that may attenuate the impact of parental alcoholism or drug addiction on their children [117]. Beyond the adverse environmental consequences associated with having a parent suffering from alcoholism, children of alcoholics (COA) may be at increased genetic risk for impulsivity and sensation-seeking related to risk variants of the serotonin transporter, dopamine receptor, and GABA receptor genes [118], among others. Several studies have also documented structural white matter differences in the brains of COAs relative to non-COAs [119–121]. Interestingly, COAs who show more resilience to developing addiction relative to their more vulnerable COA peers exhibit greater activation in the orbital frontal gyrus and left insula, areas associated with flexibility in social and emotional behaviours [120]. Examining the role of empathy and related emotional processes over time in such at-risk groups of youth could help to elucidate whether empathic capacity represents a resilience factor in addiction trajectories. If this is the case, interventions designed to enhance empathic capacity in children of substance abusers could represent a cost-effective and far-reaching preventive investment [122].

4.5 Conclusion

Mechanisms that underlie the development of substance use disorder are complex and likely to vary inter-individually. Stemming from this review of literature, we argue for more research into an understudied, yet modifiable factor—empathy—in the developmental trajectory of substance use disorders. If empathy is a protective factor, empathy-enhancing interventions could represent a powerful early preventive intervention for children and adolescents at risk for addiction. In adults who have developed substance use disorders, understanding whether deficits in empathic processing remit or persist in recovery is crucial to optimise long-term outcomes and minimize the likelihood of relapse.

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Figure 1.
Hypothesized model of how the empathic capacity spectrum may influence progression of substance use.

Figure 2.
Flow chart of studies screened, examined, and reviewed.

Table 1
Articles on empathy/theory of mind/social cognition in substance abusers versus controls (n = 19)

Author	Sample	Design	Measure(s)	Analysis/covariates	Findings	Limitations
Bosco et al., 2014 [64]	N = 22 adults (15 men, 7 women) with history of alcoholism ranging from 3 – 40 years) and 22 controls	Cross-sectional	Interview: Theory of Mind Assessment Scale	Independent samples t-test/none	Alcoholics exhibited poorer theory of mind relative to controls; among alcoholics, theory of mind ability was unrelated to duration of alcoholism or abstinence	Cross-sectional design and small sample
Bucher et al., 2013 [78]	N = 321 medical students (45 self-reported stimulant abusers; 276 non-stimulant abusers)	Cross-sectional	Self-report: Jefferson Scale of Empathy, Zuckerman-Kuhlman Personality Questionnaire	Independent samples t-test/none	No difference in empathy between stimulant-abusing and non-stimulant abusing students; stimulant abusing students scored higher on Aggression-hostility subscale of ZKPQ	No control for confounding factors, reliance on self-report of substance abuse, empathy measured only by self-report questionnaire
Dethier & Blairy, 2012 [66]	N = 68 Caucasian males (23 Type-I alcoholics; 21 Type-II alcoholics; 24 controls)	Cross-sectional	Behavioural: Benton Facial Recognition Test, emotional contagion task, mimicry task	Repeated measures ANOVA/depression and evaluative anxiety considered; depression controlled	No differences in face emotion recognition; in emotional contagion task, alcoholics (both types) expressed less joy, surprise, and arousal and more sadness and contempt relative to controls; in mimicry task, Type II alcoholics expressed more anger relative to Type I's and controls	Small sample size, no women studied
Ferrari et al., 2014 [72]	N = 102 (62 patients with drug addiction, 40 healthy controls)	Cross-sectional	Self-report: EQ	Compared total and subscale scores between drug addicted patients and controls using t-tests/none	Patients with drug addiction had lower emotional empathy compared to controls – deficits were greater for males; no difference in cognitive empathy or social skills.	No control for confounding factors, empathy measured only by self-report
Gizewski et al., 2013 [65]	N = 48 males (12 with schizophrenia, 12 schizophrenia + alcohol dependence, 12 alcohol dependence only 12 controls)	Cross-sectional	Self-report: IRI Behavioural: RMET Functional neuroimaging: fMRI during RMET	ANOVA and χ^2 tests/age and education considered	Alcohol dependence-related impairment in mind-reading limited to insular dysfunction. Relation to deficits in affective empathy is suggested.	Small sample size; co-morbid patients had significantly longer abstinence period than alcoholics without schizophrenia, no women

Author	Sample	Design	Measure(s)	Analysis/covariates	Findings	Limitations
Hulka et al., 2013 [68]	N = 106 (58 cocaine users, 48 controls)	Cross-sectional	Behavioural: Abbreviated Comprehensive Affect Testing System to assess emotional perception of facial affect, prosody, and semantic content	Linear regression analysis/age, sex, verbal intelligence quotient	Perception of discrete emotions not different between cocaine users and controls but cocaine users showed deficiencies in processing more complex emotions involving multiple verbal and non-verbal cues. Duration and severity of cocaine use was inversely related to performance.	Small sample, depression not controlled
Kim et al., 2010 [69]	N = 38 males (19 abstinent methamphetamine abusers; 19 healthy controls)	Cross-sectional	Behavioural: Visual activation paradigm Functional neuroimaging: fMRI correlates of empathic processing	Independent samples t-test, Pearson correlation analyses/none	Methamphetamine users demonstrated hypoactivation in orbitofrontal cortex, temporal poles, and hippocampus relative to controls	Small sample, educational level differed between methamphetamine abusers and controls, no women
Kim et al., 2011b [71]	N = 38 males (19 abstinent methamphetamine abusers; 19 healthy controls)	Cross-sectional	Behavioural: Fear/threat scenes from International Affective Picture System Functional neuroimaging: fMRI while viewing images	Independent samples t-test/none	Methamphetamine abusers had lower activation in bilateral insula relative to controls suggesting lower empathic concern and emotional response	Small sample, education difference between methamphetamine abusers and controls
Kim et al., 2011a [71]	N = 55 (28 methamphetamine abusers; 27 controls)	Cross-sectional	Behavioural: Facial Emotion Recognition Test, Revised RMET, Hinting Task	Independent samples t-test with Bonferroni correction/none	Methamphetamine users had poorer recognition of fearful faces, poorer theory of mind	Small sample, no control of confounders
Kornreich et al., 2002 [60]	N = 60 (30 recently detoxified alcoholics, 30 controls)	Cross-sectional	Behavioural: Emotional facial expression recognition	Repeated measures ANOVA/age, depression, anxiety, cognitive test scores considered	Alcoholics showed emotion recognition deficits for anger, disgust, sadness, and happiness relative to controls.	Small sample size
Levenson, 1990 [73]	N = 63 males (24 drug unit residents, 18 rock climbers, 21 policemen and firemen)	Cross-sectional	Self-report: Psychopathy Scale, Fantasy-Empathy Scale	ANOVA with Bonferroni correction for multiple tests/none	Drug-unit residents (antisocial risk takers) had higher antisocial orientation and lower empathy compared to rock climbers (adventurous risk takers) and policemen and firemen (prosocial risk takers)	Small sample, no control of confounders, reliance on self-report measures of empathy, no women
Martinotti et al., 2009 [74]	N = 257	Cross-sectional	Self-report: EQ	Independent samples t-test/none	Alcohol-dependent subjects had lower	Cluster B Personality Disorder and other

Author	Sample	Design	Measure(s)	Analysis/covariates	Findings	Limitations
	(150 recently detoxified alcohol dependent subjects, 107 controls)				empathy compared to controls; results appeared to be driven by differences among females.	comorbid Axis I or II disorders may have confounded findings, no control of confounders
Maurage et al., 2011 [75]	N = 60 (30 recently detoxified alcohol dependent inpatients, 30 healthy controls)	Cross-sectional	Self-report: IRI, EQ	One-way ANOVA/none	Alcoholics had lower empathic concern, personal distress, and emotional reactivity compared to controls	Small samples size; no control for confounders; reliance on self-reported empathy
Maurage et al., 2015 [63]	N = 68 (34 recently detoxified alcohol dependent inpatients, 34 healthy controls)	Cross-sectional	Self-report: IRI Behavioural: False belief task (theory of mind)	Independent samples t-tests/none	Alcohol dependent individuals scored lower on perspective-taking subscale or IRI, and exhibited poorer theory of mind ability compared to controls	Small samples size; no control for confounders; reliance on self-reported empathy
Mohagheghi et al., 2015 [76]	N = 80 (40 alcohol dependent outpatients, 40 inpatients without mental illness)	Cross-sectional	Self-report: Bar-On Emotional Intelligence Questionnaire	Independent samples t – test/none	Alcohol-dependent subjects had lower empathy scores compared to controls.	Small sample size, confounders not controlled, reliance on self-reported empathy
Nandrino et al., 2014 [61]	N = 80 (50 alcohol dependent patients, 30 controls)	Cross-sectional	Behavioural: V-SIR Reading, RMET (both theory of mind tests)	Student's t-test/none	Alcohol dependent patients showed poorer theory of mind on the RMET, but not the V-SIR	Small sample size, confounders not controlled
Porcerelli et al., 1995 [77]	N = 36 male weight lifters (16 anabolic steroid users, 20 non-steroid using weight-lifters)	Cross-sectional	Self-report: Narcissistic Personality Inventory	ANOVA/none	Steroid had lower self-rated affective empathy compared to non-steroid-using weight-lifters	Small sample size; self-report of steroid use; high attrition rate for anabolic steroid users; no women
Preller et al., 2014 [67]	N = 168 (100 cocaine users, 68 healthy controls)	Cross-sectional	Behavioural: MET, MASC, RMET	ANCOVA, MANCOVA/age, education	Cocaine users had lower emotional empathy compared to controls; cognitive empathy not different; younger age of onset of cocaine use associated with more pronounced empathy impairment	No control for depression
Thoma et al., 2013 [62]	N = 40 (20 recently detoxified alcohol dependent patients, 20 healthy controls)	Cross-sectional	Self-report: IRI Behavioural: Revised RMET, Faux Pas Story Test	ANCOVAS with Bonferroni-correction/depression	Alcohol dependent patients had lower cognitive empathy than the control group as measured by the RMET and Faux Pas Story Test; no difference found on self-reported empathy	Small sample size; trend towards difference in education between alcoholics and controls

ANOVA, analysis of variance; EQ, Empathy Quotient; fMRI, Functional magnetic resonance imaging; IRI, Interpersonal Reactivity Index ; RMET, Reading the Mind in the Eyes Test; V-SIR, Versailles-Situational Intention; ZKPQ, Zuckerman–Kuhlman Personality Questionnaire.

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Table 2

Articles on empathy and substance-related behavior (n = 4)

Author	Sample	Design	Measure(s)	Analysis/covariates	Findings	Limitations
Jurkovic, 1979 [88]	N = 52 self-reported drug users	Cross-sectional	Self-report: Hogan abbreviated empathy scale	Bivariate correlation analysis on empathy and drug use behaviour (total use, frequency, social complications)/none	No relationship between empathy and drug use behaviour	Small sample size, reliance on self-report measure of empathy; did not control for confounders
Massey et al., 2015b [12]	N = 143 Caucasian women oversampled for pregnancy smoking	Cross sectional	Behavioural: Diagnostic Analysis of Nonverbal Accuracy-2	Linear regression analysis/amount smoked prior to recognition of pregnancy, prenatal alcohol and drug use, impulsivity, depression, education, income	Impaired accuracy in identifying sad, fear, and anger faces associated with higher levels of smoking among women with oxytocin receptor gene (OXTR) variants rs53576 (GG) and rs2254298 (A)	Face processing task was performed <i>after</i> pregnancy when smoking was measured, results only applicable to pregnant women
McCown, 1989 [90]	N = 97 Twelve Step group attendees	Cross-sectional	Self-report: Eysenck's Impulsivity Inventory	Bivariate correlation analysis/none	Higher empathy was correlated with greater hours of Twelve Step activity, months abstinent, and total months in self-help throughout lifetime	Reliance on self-reports of abstinence and empathy, no control for confounders
Nguyen et al., 2011 [86]	N = 498 African-American adolescents	Cross-sectional	Self-report: Bryant's Index of Empathy in Children and Adolescents	Structural equation modelling/none	Empathy positively correlated with drug refusal efficacy (likelihood to refuse drugs in various situation measured by the Specific Event Drug and Alcohol Refusal Efficacy scale); drug use efficacy mediated link between empathy and lower past 30 day drug use	Low reliability coefficient for empathy measure; reliance on self-report data, no control for confounders

Table 3

Articles on empathic deficits and substance use (n = 14)

Author(s)	Sample	Design	Empathic deficits measure	Analysis/covariates	Findings	Limitations
Baskin-Sommers et al., 2015 [85]	N = 1,170 male felony offenders ages 14 – 18	Longitudinal	<u>Self-report</u> : YPI annually over a 5 year period	Negative binomial regression/school drop-out, intelligence, emotion regulation, anxiety, family arrests, peer deviance, neighbourhood conditions, single-parent household	CU traits predicted substance use above and beyond baseline level of use, and individual, peer and family-level factors covariates.	Reliance on self-report for all measures of relevance to current review, no women
Colins et al., 2015 [82]	N = 417 non-referred men	Longitudinal	<u>Self-report</u> : YPI – affective and interpersonal dimensions	Logistic regression analysis/age, race, ethnicity, prior reported alcohol and marijuana use	YPI dimensions did not predict excessive alcohol or marijuana use	Reliance on self-report for measures of psychopathy and substance use
Durbeej et al., 2014 [93]	N = 134 Swedish adult offenders (93 females) with mental health and co-occurring problematic substance use	Cross-sectional	<u>Semi-structured interview</u> : PCL-R affective facet (lack of empathy, shallow affect)	Hierarchical logistic regression to examine relationship between facets of psychopathy and (1) participation in outpatient substance abuse treatment appointments and (2) dry housing residence/severity of drug, social, family, and legal problems; interpersonal, lifestyle, and antisocial facets of psychopathy	The affective facet of psychopathy (lack of empathy, shallow affect) independently predicted lack of participation in outpatient substance abuse treatment and voluntary residence in dry housing	Cross-sectional design
Gustavson et al., 2007 [91]	N = 100 adult violent offenders (92 men, 8 women)	Cross-sectional	<u>Semi-structured interview</u> : PCL-R, deficient affective experiences factor	Non-parametric Whitney-Mann comparisons/none	Deficient affective experience was associated with lower age of onset of substance abuse, but not years of abuse	Cross-sectional design, did not control for other psychopathy factors
Hemphälä et al., 2014 [83]	N = 145 substance abuse treatment seeking adolescent (86 girls, 61 boys)	Longitudinal	<u>Semi-structured interview</u> : PCL- Youth Version - affective factor (lack of remorse, shallow affect, lack of empathy, and failure to accept responsibility)	Logistic regression analysis to determine the relationship between facets of psychopathy at treatment initiation and substance use disorder 5 years later – four facets of psychopathy entered together as predictors/sex, number of conduct symptoms	Empathic deficits in adolescence did not predict substance use disorder 5 years after initiation of treatment in men or women.	Small sample size relative to number of predictors modelled,
Hillege et al., 2010 [87]	N = 776 Dutch non-referred adolescents mean age 16 years, 53% female	Cross-sectional	<u>Self-report</u> : YPI – CU dimension	Correlation analysis comparing High CU/High CP, High CU/Low CP, and Low CU/High CP groups on drug and alcohol use disorders	Individuals with High CU traits had highest prevalence of alcohol and drug use disorders	Cross-sectional design, no covariates

Author(s)	Sample	Design	Empathic deficits measure	Analysis/covariates	Findings	Limitations
Hyde et al., 2015 [80]	N = 268 low income men ages 17 – 20	Longitudinal	Self-report: APSD	Logistic regression analysis used to determine predictive value of CU-traits at age 17 on substance abuse and dependence diagnoses at age 20/rule-breaking and aggression	CU traits at age 17 predicted substance dependence diagnosis at age 20.	Women not included in this study.
Neumann et al., 2008 [89]	Community sample of N = 514, ages 18–40, 196 men, 318 women	Cross-sectional	Semi-structured interview: PCL-SV Affective dimension	Correlation analysis/n[93]one	Affective dimension correlated with alcohol use in white men, not in women or African Americans	Cross-sectional design
Patrick et al., 2005 [94]	N = 219 male federal prison inmates	Cross-sectional	Semi-structured interview: PCL-R, affective/interpersonal factor, also affective factor alone	Partial correlation of factor with smoking, controlling for externalizing behaviour	Affective factor alone was related to smoking, but not when externalizing behaviour is controlled.	Cross-sectional design, no women
Reardon et al., 2002 [95]	N = 329 male federal prison inmates	Cross-sectional	Semi-structured interview: PCL-R, Emotional Detachment factor	Regression analysis/age	Emotional detachment was unrelated to alcohol problems.	Cross-sectional design, no women
Schulz et al., 2016 [96]	N = 318 men and women with past 6 month illicit drug use, and past year criminal history	Cross-sectional	PCL-SV, interpersonal/affective facet	Hierarchical multiple regression analysis/age, ethnicity, childhood adversity, borderline personality disorder, caregiver demographics; gender as hypothesized moderator	Interpersonal/affective factors associated <i>fewer</i> reported drug abuse symptoms, and in women, with later age of onset of drug use.	Cross-sectional design, reliance on self-reports of drug use
Swogger et al., 2016 [84]	N = 105 adults (68 men, 37 women) in a pretrial jail diversion program	Longitudinal	Semi-structured interview: PCL-R, affective facet	Regression analysis/baseline percentage days abstinent, other facets of psychopathy, and race/ethnicity	Affective facet predicted fewer days abstinent, and less benefit from brief motivational interviewing at 6 month follow up	Analysis of distinct facets was exploratory, significant participant attrition
Walsh et al., 2007 [92]	N = 399 male county jail inmates, 190 African-Americans, 209 European Americans	Cross-sectional	Semi-structured interview: PCL-R, callous interpersonal style and deficient affective experience facets	Regression analysis/antisocial personality disorder symptoms and antisocial facet of psychopathy	Callous interpersonal style <i>positively</i> related to substance use disorders; deficient affective experience facet was <i>inversely</i> related to substance use disorders.	Cross-sectional design

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Author(s)	Sample	Design	Empathic deficits measure	Analysis/covariates	Findings	Limitations
Wynns et al., 2012 [79]	N = 521 sixth-graders followed through 9 th grade	Longitudinal	Self-report & Parent report. APSD, CU items only	Hierarchical logistic regression/age, gender, depressive symptoms, family history of substance use, conduct disorder symptoms	Parent-reported, not self-reported CU traits predicted increased likelihood of alcohol and marijuana use, recurrent use, and impairment, when accounting for conduct disorder symptoms.	Low levels of substance use in sample

APSD, antisocial process screening device; CP, conduct problems ; CU, callous-unemotional; PCL-R, Hare Psychopathy Checklist-Revised; PCL-SV, Hare Psychopathy Checklist Screening Version; YPI, Youth Psychopathic Traits Inventory.