

Preference for Immediate Rewards in Attention-Deficit/Hyperactivity Disorder and Substance Use Disorder: A Shared Intermediate Phenotype?

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Abstract

Purpose of Review This brief review explores to what extent ADHD and SUD are both associated with reward-related impulsivity, operationalized as steep delay discounting (DD). However, an integrated view on DD as a potentially shared intermediate phenotype for these frequently co-occurring conditions is lacking.

Recent Findings Though mostly studied in separate conditions, some studies have investigated DD specifically in patients with co-occurring conditions of SUD and ADHD. In addition to reviewing literature that has documented the associations between ADHD and relatively steep DD and between SUD and relatively steep DD, we also reviewed more recent literature in which steep DD has been examined as a transdiagnostic mechanism.

Summary Overall, literature on DD in SUD suggests a dose-response relation between SUD severity and DD. The literature suggests that relatively steep DD is a mechanism associated to (ab)use of a range of substances. As for the link between DD and ADHD, several meta-analyses reported steeper DD in individuals with ADHD than controls (medium effect sizes). Because these bodies of literature are based on studies in which the influence of comorbidity was not assessed, it is hard to conclude that relatively steep DD is *directly* related to the ADHD symptoms per se, or to the SUD per se. Therefore, a close inspection of more recent literature in which comorbidity was taken into account, and DD was treated as a transdiagnostic mechanism, was included here. Based on this reviewed recent work, we propose a model about the nature of the co-occurrence of ADHD, SUD, and DD. Implications of the nature of co-occurring ADHD, SUD, and relatively steep DD for prevention and intervention strategies are discussed.

Keywords Substance use disorder \cdot Attention-deficit/hyperactivity disorder \cdot Delay discounting \cdot Immediate reward \cdot Comorbidity \cdot Intermediate phenotype

Introduction

Substance use disorder (SUD) is a prevalent psychiatric disorder that often co-occurs with other psychiatric disorders, including attention-deficit hyperactivity disorder (ADHD).

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Both genetic and environmental factors contribute importantly to SUD [1].

Heritability is estimated to be around 50% [2]. Whereas genetic factors are thought to play an important role in the transition from substance use to SUD, environmental factors seem to contribute to exposure and substance use initiation [3, 4•, 5]. Individuals with SUD demonstrate compulsive substance seeking, causing impaired functioning [6]. The prevalence of SUD among adults is ~4–5% [7].

ADHD is also a prevalent psychiatric disorder [8], with a strong heritability estimated at around 74–80% [9, 10]. Siblings and children of individuals with ADHD have an eightfold increased risk for ADHD [11, 12]. Individuals with ADHD experience levels of inattention and/or hyperactivityimpulsivity that interfere with their daily functioning [6]. The prevalence of ADHD is $\sim 7\%$ [13] in children/adolescents, and $\sim 2.5-4.4\%$ in adults [14, 15].

ADHD and SUD frequently co-occur. Among adults with a diagnosis of ADHD, 35% were found to have been diagnosed with SUD [16]. Conversely, among individuals with a diagnosis of SUD, 23% of individuals meet criteria for ADHD [17]. Several mechanisms driving this frequent comorbidity have been suggested. ADHD might increase the risk of using addictive substances. For instance, some addictive substances have been suggested to alleviate ADHD symptoms, at least in the short term [18-20]. Substance use might also contribute to persisting ADHD into adulthood [21], while other causal factors may predispose to both ADHD and SUD. For instance, shared genetics or traumatic experiences have been shown to contribute to both conditions [22•]. Indeed, several studies suggest that people with ADHD and people with SUD share certain premorbid underlying vulnerabilities at the psychological and neural level, like reward processing deficits (e.g., [23, 24]).

This brief review explores to what extent ADHD and SUD are both associated with reward-related impulsivity, operationalized as relatively steep delay discounting (DD). Delay discounting (for a review, see [25]) refers to the phenomenon that the subjective value of rewards decreases as a function of waiting time. The further into the future a reward will be delivered, the lower the subjective value of that reward. This phenomenon plays a role in daily decisions requiring trade-offs between anticipated benefits and costs of two options at different points in time. For example: Should I spend all my saved money now on a new car, or should I save longer and buy an even better car 2 years from now? In experimental lab settings, DD tasks are used to measure these preferences, by presenting people with choices between small immediate and larger delayed rewards. Relatively steep DD, expressed by relatively strong preferences for small immediate rewards, is associated with psychiatric disorders characterized by atypical impulse control, including ADHD and substance abuse [25], and as such it can be viewed as a "risk index" for ADHD and substance abuse.

Though mostly studied in separate conditions, some studies have investigated DD specifically in patients with co-occurring conditions of SUD and ADHD. However, an integrated view on DD as a potentially shared intermediate phenotype for these frequently co-occurring conditions is lacking. In addition to reviewing literature that has documented the associations between ADHD and steep DD and between SUD and relatively steep DD, we also reviewed more recent literature in which relatively steep DD has been examined as a transdiagnostic mechanism. Based on the literature, we propose a model about the nature of the co-occurrence of ADHD, SUD, and DD. Implications of the nature of co-occurring ADHD, SUD, and relatively steep DD for prevention and intervention strategies are discussed.

Delay Discounting in Relation to SUD and ADHD

Substantial, largely separate, bodies of empirical literature exist on the question whether individuals with ADHD engage in impulsive decision-making, and whether individuals with SUD engage in impulsive decision-making, as reflected by steep delay discounting. This is typically measured with DD tasks. Both experiential (money is paid and delays are endured) and hypothetical (money is not paid and delays are not endured) tasks have been used. In experiential tasks, participants may be asked: Would you rather receive 2/4/6/8 cents now or 10 cents after 5/10/20/30/60 s? In hypothetical tasks, participants may be asked: Would you rather receive 100/200/300/400/500 etc. euros today or 1000 euros after 1/2/6/12 months? See for an overview of DD task types [25].

Relatively Steep Delay Discounting in Individuals with SUD

Many studies published before 2018 examined the relation between SUD or substance use and delay discounting. In a meta-analysis, Mackillop and colleagues included both clinical and subclinical samples of addiction and reported significant associations between delay discounting and addictive behaviors, with small effect sizes [23]. However, a separate analysis showed larger effect sizes (i.e., medium) for clinical versus non-clinical samples. In another meta-analysis, Amlung and colleagues indicated a significant relation with a small effect size between delay discounting and continuous measures of addiction severity and quantity frequency of use in both clinical and non-clinical samples [26]. Findings were comparable across experiential and hypothetical tasks. Moreover, both included studies in substance use (alcohol, drugs, tobacco) and gambling and reported no difference in delay discounting across types of addiction in clinical and subclinical samples. Indeed, a review published in 2018 concluded no differences in delay discounting across drug of choice [27]. Yet, the number of studies directly comparing different substance classes was limited.

In a more recent meta-analysis, Kluwe-Schiavon et al. [28•] found steeper discounting of delayed rewards in SUD patients (alcohol, drugs) compared with controls, with moderate to large effect sizes. The fact that this metaanalysis only included clinical samples may explain the larger effect sizes than those reported earlier. Compatible with previous studies, there were no robust differences in delay discounting across different substances. Importantly, results showed that early onset of substance use and psychiatric comorbidities were linked to stronger effects on delay discounting. Of note, the vast majority of the studies included in this meta-analysis were published before 2018.

More recent studies also report positive associations between the extent of cannabis use and delay discounting [29]. Additionally, smokers have been reported to demonstrate steeper DD than non-smokers [30], and the same goes for individuals with nicotine dependence compared to controls [31]. However, previous findings of early age of SU onset as an amplifier of the link between relatively steep DD and SU frequency were not replicated recently. For example, Parlar et al. (2021) reported that the significant but weak association between cannabis use and relatively steep DD was not amplified by early age of onset [32]. Additionally, in one study [33], the reverse pattern was found, as late-onset(18 years), but not early-onset (13 years) smokers compared to controls were found to show relatively steep DD. When early and late-onset smokers were compared to one another directly, they did not differ in DD.

Overall, literature on delay discounting in SUD suggests severity-dependent effects and may suggest that relatively steep DD is a mechanism associated with (ab)use of a range of substances. An explanation that has been put forward for the severity effect (especially relatively steep DD observed in frequent users) is that relatively steep DD is not linearly associated with substance use, but rather that relatively steep DD is a risk factor specifically for *high-level use* of substances [34•]. This links to the reported findings that a clinical diagnosis of SUD is more strongly associated with relatively steep DD than subclinical levels of substance use [23, 26].

Relatively Steep DD in Individuals with ADHD

Four meta-analyses reported findings of studies in which ADHD groups were compared with control groups on delay discounting [24, 35–37]. All meta-analyses reported steeper delay discounting in individuals with ADHD than controls, with generally speaking medium effect sizes. There was some evidence that the ADHD-control difference was larger in (young) children than in adolescents or adults [36, 37].

In terms of moderators, Marx et al. reported that the relative preference for immediate rewards in the ADHD groups was substantially less in studies that used real rewards compared to studies that used hypothetical rewards [35]. Patros et al. [36] reported that group differences were larger in male-only samples than in mixed-gender samples. This may suggest that steep DD is more pronounced in males with ADHD than females with ADHD, or it may be due to the fact that females are more often diagnosed with ADHD-inattention, and inattention may be less strongly associated with relatively steep DD. Note, however, that in a follow-up study with larger samples of girls with ADHD-combined type, and with real DD tasks, especially girls (and not boys) with ADHD demonstrated relatively steep DD. More research is needed to further clarify the influence of task type, ADHD symptom domain, and gender on the association between ADHD and relatively steep DD. Additionally, and very relevant here, the vast majority of studies included in the meta-analyses did not exclude participants with comorbid diagnoses, including SUD. Obviously, this makes it hard to conclude that relatively steep DD as observed in individuals with ADHD is *directly* related to the ADHD symptoms per se.

Thus, most findings of relatively steep DD in individuals with ADHD and in individuals with substance abuse are based on studies that did not assess the influence of comorbid symptoms, but rather studied ADHD and substance abuse separately in relation to DD. Given that ADHD and substance abuse are frequently comorbid, it is not clear as of yet whether relatively steep DD as associated with ADHD may result from comorbidity with substance abuse, and whether relatively steep DD as associated with substance abuse may result from comorbidity with ADHD. It is an empirical question whether relatively steep DD in ADHD is in part a function of unmeasured SUD, and whether relatively steep DD in SUD is in part a function of unmeasured ADHD. Therefore, it is worth trying to understand how DD is implicated when ADHD and substance abuse co-occur within individuals.

Recent Research Addressing DD in Relation to the Conjunction of ADHD and SUD

More recently, researchers have started examining DD in relation to ADHD and SUD in the same individuals. For example, Parlar and colleagues studied to which extent cannabis use was associated with DD and with ADHD symptoms, in a large sample of high-drinking emerging adults [32]. They found that cannabis use was significantly (but weakly) associated with relatively steep DD and with ADHD symptoms. *How* these three are inter-related remains as of yet unclear. Parlar et al. suggested that based on shared genetic factors between ADHD and cannabis use [38], ADHD may be a risk factor for cannabis use. However, the directionality of the association between ADHD, SUD, and DD still needs to be addressed in future research.

Similarly, Petker and colleagues [34•] selected bingedrinking emerging adults, and within this sample, they compared daily, occasional, and no-cannabis users with one another. The daily cannabis users reported more hyperactivity-impulsivity symptoms (but not inattention symptoms) and steeper DD than the other two groups. The same group of researchers [39] published data from another sample, consisting of community adults, and reported that the severity of cannabis use was associated with greater endorsement of ADHD symptoms and relatively steep DD. Because both studies are cross-sectional, the directionality or causality of these associations remains unclear.

While the studies by Parlar and Petker examined relations between SUD, ADHD, and DD within the same individuals, they did not examine whether ADHD or SUD was uniquely associated with relatively steep DD, by controlling for the comorbid symptom dimension. This is what Paraskevopoulou and colleagues (2020) did [40•]. They found that after accounting for family history of substance misuse, individuals with ADHD and substance misuse had steeper DD than ADHD individuals without substance misuse. However, individuals with ADHD only (and no substance misuse) did not have steeper DD than controls. This suggests that substance misuse (in ADHD) may be more strongly/directly associated with DD than ADHD per se, and that previously reported associations between ADHD and relatively steep DD may be (partly) explained by comorbid substance (mis) use in a subgroup of patients. It needs to be noted that findings by Patros et al. and Pauli-Pott et al. [36, 37] show that the association between relatively steep DD and ADHD was strongest in younger age groups, in which there was no comorbid substance use. Possibly, for children with ADHD who have relatively steep DD, the risk for developing later substance use may be higher (see Fig. 1 where relatively steep DD acts as a moderator of the link between ADHD and substance use).

In general, a transdiagnostic and dimensional view of psychopathology has received more attention recently [41, 42, 43••], and relatively steep DD may be viewed as a transdiagnostic mechanism involved in multiple behavioral expressions such as SUD and ADHD [43••, 44••]. Levitt and colleagues (2022) investigated DD as a transdiagnostic measure for numerous psychopathological dimensions,

conducting both individual and simultaneous analyses in a large community sample $[43 \bullet \bullet]$. Higher DD was related to ADHD, drug, tobacco and cannabis misuse, anxiety, depression, and PTSD. It was not found for alcohol misuse. However, in concurrent analyses, allowing to examine which psychopathology dimensions correlated with relatively steep DD over and beyond their correlations with other symptom dimensions, significant positive associations with DD were found only for tobacco and cannabis misuse and depression. ADHD and alcohol misuse did not show a significant relation with DD.

In line with this research, Oddo et al. (2021) attempted to clarify which reward components are specific to ADHD and alcohol use disorder and which are shared $[45 \bullet \bullet]$. This was examined in a community-based sample of young adults. In contrast to previous literature, relatively steep DD was not significantly related with ADHD, alcohol use disorder, and their underlying shared symptom dimensions. Possibly, this was due to the fact that only mild levels of symptoms were present in this sample, and/or due to the fact that the short and hypothetical DD task did not sufficiently tap into delay aversion. Interestingly, "environmental suppressors" (lower reward access) significantly correlated with alcohol use disorder and the underlying ADHD-alcohol use disorder shared dimension. This raises the possibility that easy access to substances is an important moderator that determines the extent to which individuals with ADHD symptoms will end up (ab)using substances.

Recently, DeRosa et al. (2022) examined DD in a psychiatric sample of over 1800 children and adolescents [44••]. They took a developmental perspective by looking at agerelated changes (cross-sectional design), and used multiple monetary DD tasks with each employing a different amount of the large delayed reward, as well as a food DD task.

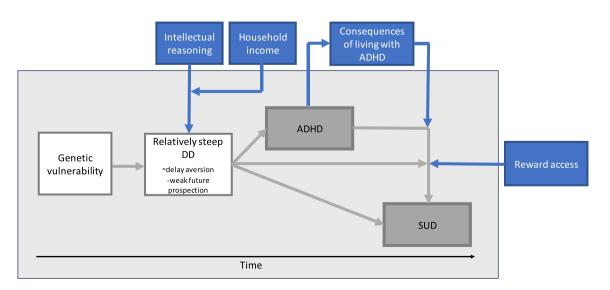


Fig. 1 Model of the nature of co-occurrence of ADHD and SUD, and the role that DD may play in this

Individual diagnostic groups were compared to a control group. As for ADHD, it was shown that ADHD-combined type was associated with age-constant relatively steep DD on the money task. When transdiagnostic subtype profiles were examined, it turned out that especially a subtype of ADHDinattentive/learning disorder/low cognitive-academic scores and a subtype of ADHD-combined/anxiety disorders/emotional-behavioral problems were associated with relatively steep DD. Importantly, a strong and negative association between relatively steep DD and intellectual reasoning was found, and when intellectual reasoning was low, low household income magnified the association between low intellectual reasoning and relatively steep DD. It suggests that DD may be particularly steep in children/adolescents with psychiatric disorders who come from a family with low household incomes. This sample did not include substance (ab)use likely due to the age range used, but the approach is very promising and can be used in the future when aiming to gain more insight into ADHD-SUD comorbidity and the nature of its associations with relatively steep DD, taking contextual factors into account.

Integration and Discussion

Taken together, relatively steep DD has been associated with both ADHD and SUD, but the exact causal nature of this relation needs further transdiagnostic exploration, based on longitudinal data. Based on the findings so far, we propose a model on the nature of the co-occurrence of these behavioral manifestations of relatively steep DD within individuals, which further extends the shared underlying mechanism model. Specifically, a number of nuances have been added to the model in which genetic vulnerability and relatively steep DD form shared underlying mechanisms to ADHD and SUD. For example, the fact that SUD often has a later onset than ADHD (whether this is primarily determined by reward access or by inherent developmental processes is still an empirical question) is acknowledged in this model. It may well be that ADHD is expressed at an earlier age than SUD, because children are exposed to environments requiring attention and impulse control at an earlier age (e.g., in classrooms) than environments that trigger substance use. Additionally, recent findings as reviewed above would need to be incorporated into a plausible model. For example, Paraskevopoulou and colleagues [40•] published findings that suggest that the association between ADHD and relatively steep DD may be indirect, because relatively steep DD was mainly associated with comorbid cases and not with ADHD only.

We propose a model that hypothesizes about the nature of the interrelations between ADHD, SUD, and DD over time. We propose that individuals' initial risk of developing ADHD and/or SUD is determined by genetic and early environmental factors [46•]. Based on the fact that SUD generally has a later onset than ADHD (ADHD has by definition an age of onset < 12), and based on the fact that ADHD is strongly associated with relatively steep DD in early childhood [36, 37], due to genetic and early environmental factors, we speculate that ADHD predisposes to SUD, potentially through the preference of immediate rewards in a subset of ADHD individuals. Specifically, SUD may be one way to cope with the negative consequences of ADHD, such as receiving frequent criticism and experiencing stigma [19, 47•, 48, 49, 50•], experiences of failure [51], and low self-esteem [51, 52]. In fact, qualitative research has shown that individuals with ADHD report using substances as a way to feel stable [20], or to feel respected and accepted [53]. Therefore, a specific prediction would be that the more negative consequences people with ADHD experience, the more likely they are to develop SUD. Using substances may be viewed as a non-effective way to cope with negative feelings among those with ADHD [54•].

Furthermore, relatively steep DD is viewed as a moderator of the association between ADHD and SUD: in those individuals with ADHD who have relatively steep DD, the likelihood of substance use increases, because of immediately rewarding experiences following substance use. This would be supported by the finding that individuals with ADHD who use prescribed medication have a lower risk of developing SUD [55]. Based on recent research [45••], a moderator of the longitudinal association between ADHD and SUD was suggested to be reward access: the easier the access, the more likely individuals with ADHD end up using substances.

In sum, in early childhood, ADHD is associated with relatively steep DD, and those with relatively steep DD have a higher likelihood of developing SUD over time. Then, once SUD has developed, the drug use further reinforces relatively steep DD and vice versa. This might also explain the association between SUD and ADHD persistence [21]. Importantly, the likelihood that children and adolescents with psychiatric disorders showed relatively steep DD was higher when intellectual reasoning abilities were lower. Household income was a further exacerbating factor, which was especially so for youngsters with ADHD-inattentive type [44••]. It needs to be considered that for youngsters growing up in families with low household incomes, it may be adaptive to take an immediate reward because it is certain [56•].

People may show relatively steep DD for various different reasons. In other words, relatively steep DD may be viewed as a behavioral manifestation that we can measure, which associates with ADHD and SUD and is driven by various factors and internal motives that vary across individuals. It is important to understand these factors and internal motives, so as to be able to intervene in relatively steep DD. This opens new perspectives for prevention.

One important motive for relatively steep DD in individuals with ADHD is delay aversion [57–59]. Aversive feelings are associated with having to wait for a motivation for wanting to escape delays, and this expresses as a relatively strong preference for small immediate rewards [60]. Another motive for relatively steep DD may be weak future thinking [61]. If the focus is less on the future and more on the now, then that may contribute to relatively steep DD. When delay aversion is an important contributing factor to relatively steep DD, interventions that help individuals tolerate aversive feelings (e.g., mindfulness [62•]) would be likely successful in reducing relatively steep DD, and potentially preventing the development of SUD in youth with ADHD. When weak future prospection is an important factor in relatively steep DD, then interventions that help individuals focus on the future and bring the future to the now (e.g., episodic future thinking [62•]) are likely to be successful in reducing relatively steep DD.

In SUD, it has been suggested that working memory may play a significant role in relatively steep DD [63], and an initial study reported that working memory training was associated with DD reductions in individuals with SUD [64]. Scholten and colleagues suggested in their review of DD-reducing strategies that acceptance-based/mindfulnessbased trainings as well as trainings or manipulations involving future orientation held the greatest promise [62•]. At the same time, while these trainings and manipulations have been proven to be effective at reducing DD on lab tasks, generalization to reductions in real-life impulsive behaviors such as smoking is as of yet limited.

Based on further evidence, prevention and intervention approaches can be tailored. If relatively steep DD increases the likelihood of the development of SUD in individuals with ADHD, then targeted prevention approaches could aim at reducing relatively steep DD. Based on the internal motives that contribute to relatively steep DD, such high-risk individuals may possibly benefit from certain trainings such as mindfulness or future prospection [62•]. Importantly, it will need to become clear whether previously observed training-induced reductions in DD as measured in tasks will translate to daily life behaviors.

Before concluding, we would like to address some limitations and caution. First, relatively steep DD, while often viewed as an index of impulsivity, is not necessarily a shortcoming or a deficit. It may be better viewed as a motivational style (see for example [60]), as a unique way of maximizing utility (see for relevant discussion [65]), and in certain situations as an adaptive strategy [56•]. And while it is viewed as a potentially core process involved in ADHD and SUD, one needs to be aware that effect sizes are small to moderate (see for a critical appraisal [66•]). Therefore, relatively steep DD may be considered as one of many core processes involved in ADHD and SUD and its comorbidity, in interaction with genetic, developmental, and environmental factors. It could be that relatively steep DD is one "risk factor," that, in interaction with other environmental and developmental processes, contributes to various (mal)adaptive outcomes (multifinality). Another critical point (made by [66•]) is that the generalizability of relatively steep DD as measured in the lab to decision processes in daily life is limited, and this needs to be kept in mind. Finally, DD has been involved in many other psychiatric conditions than ADHD and SUD, which do frequently also co-occur, such as conduct disorder, psychopathy, and mood disorders. Future studies should therefore study DD in ADHD and SUD, with a wider scope on co-ocurring psychopathology.

Conclusion

In conclusion, current evidence shows that both ADHD and SUD are associated with relatively steep DD. We propose a model that extends the shared underlying mechanism model, in which relatively steep DD acts as a moderator in the longitudinal association between ADHD and SUD. Once SUD has been developed, the drug use is hypothesized to further reinforce relatively steep DD, and vice versa. Various other factors including reward access, consequences of living with ADHD, reasoning ability, and household income are proposed to play key roles in the unique developmental pathway of each individual.

Author contributions All authors wrote the main manuscript. Authors A.S and A.S. prepared the figure.

Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent N.A.

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