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BRIEF REPORT

Delay Discounting Is Greater Among Drug Users Seropositive for Hepatitis C but Not HIV

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Objective: Substance dependent individuals (SDIs) typically overvalue immediate and undervalue (discount) delayed rewards, and level of discounting significantly predicts posttreatment relapse and other behavioral outcomes. Delay discounting has potential significance for studies of HIV prevention and adherence to antiretroviral therapy; but effects of HIV infection on delay discounting rates among SDIs are not well understood, although discounting rates are higher among individuals infected with hepatitis C virus (HCV). In this study, we investigated potential additive or interactive effects of HIV and HCV infection on delay discounting performance among a group of 239 SDIs with verified HIV and HCV serostatus. ***Method:*** All participants were verified abstinent from drugs and alcohol at testing. All participants completed measures of substance abuse characteristics and comorbid disorders, and the Monetary Choice Questionnaire, a well-known measure used to derive *k* coefficients, which index discounting rates. ***Results:*** Groups were comparable on demographic, substance use, and comorbid characteristics. Compared with uninfected controls, discounting rates were significantly higher among individuals seropositive for HCV but not HIV. Additionally, no significant group differences in discounting rates were observed among HCV+ participants with or without coinfection with HIV. Group differences could not be attributed to aging or nonspecific effects of drug addiction. Additionally, increased discounting rates were associated with riskier injection practices. ***Conclusions:*** Potential mechanisms contributing to this discrepancy in discounting rates between HIV+ and HCV+ SDIs, including decision making, are discussed and await further study.

Keywords: HIV, hepatitis C, drug abuse, neurocognition, delay discounting

Substance dependent individuals (SDIs) tend to make impulsive choices that favor more the prospect of attractive immediate rewards rather than a positive outcome in the future (Bechara, Damasio, Tranel, & Damasio, 1997). This bias toward choices with immediate (as opposed to future or delayed) outcomes is evident among SDIs even when a larger reward is available if the subject chooses to wait. This pattern of steep intertemporal choice or increased *delay discounting*, the tendency to devalue delayed rewards, has been demonstrated in numerous studies of individuals dependent on various substances, including cocaine, methamphetamine, and opioids (Bickel, Koffarnus, Moody, & Wilson, 2014) as well as nondrug using groups with disinhibitory behavior disorders (Paloyelis, Asherson, Mehta, Faraone, & Kuntsi, 2010). Further, studies have linked increased discounting rates with key substance use treatment outcomes, including relapse (Sheffer et al., 2014).

The construct of delay discounting has added significance for SDIs living with HIV/AIDS as a potential contributing mechanism of risky sexual and injection practices (Sheffer et al., 2014) as well as poor adherence with antiretroviral therapy. However, few studies have investigated discounting performance among HIV−seropositive (HIV+) individuals with or without substance use disorders. An important study by Meade and colleagues investigated neural mechanisms of discounting performance using functional magnetic resonance imaging (fMRI) in a group of 39 HIV+ individuals (Meade, Lowen, MacLean, Key, & Lukas, 2011). They reported that HIV+ individuals who had recently used cocaine

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showed significantly higher discounting rates and decreased activation in frontoparietal cortex compared with HIV+ individuals with previous or no cocaine use. All participants in the Meade study were HIV+, raising the question if a positive HIV serostatus is associated with higher discounting rates compared with HIV− risk-matched controls.

Infection with the hepatitis C virus (HCV) is highly prevalent among SDIs and potential effects of HCV or HIV and substance use on discounting rates might increase risk of virus superinfection, exposure or transmission by augmenting the propensity toward risky sexual and injection practices. Huckans and colleagues reported increased discounting rates among HCV-seropositive (HCV+) compared with HCV− individuals (Huckans et al., 2011). Additionally, cognitive impairment is significantly more common among individuals coinfected with HIV and HCV compared with monoinfected and uninfected individuals (Cherner et al., 2005; Hilsabeck, Castellon, & Hinkin, 2005; Martin-Thormeyer & Paul, 2009).

The aim of the present study was to investigate the potential separate or additive effects of HIV and HCV on delay discounting performance in a sample of SDIs. Study results have potential clinical significance: cognitive enhancement training can improve delayed discounting among SDIs (Bickel et al., 2011). SDIs with concurrent HIV or HCV infection may derive additional benefit from substance abuse treatment programs incorporating these techniques. The results of this study may help to identify which group (HCV+ or HIV+) will benefit most from this type of intervention to modify risk-taking behavior and prevent coinfection or relapse.

Method

Participants

We tested a group of 168 men and 71 women enrolled in a larger study of neurocognitive effects of HIV and drug abuse. The study was approved by the Institutional Review Boards for the University of Illinois and Jesse Brown Veterans Affairs Medical Center (VAMC). All subjects met *Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition* (*DSM-IV*) criteria for cocaine or opioid dependence as determined by the Structured Clinical Interview for *DSM-IV* Substance Abuse Module (SCID-SAM; First, Spitzer, Gibbon, & Williams, 1997). The sample included 68 HIV+ and 171 enzyme immunoassay (EIA)-verified HIV− participants recruited from infectious disease and substance abuse programs at the UIC, the Jesse Brown VAMC, and from the community. All subjects reported active substance use during the previous year but were verified abstinent at testing by breathalyzer and rapid urine toxicology screening for opioids, cocaine, and methamphetamine.[1] Potential study subjects with AIDS defining or other central nervous system (CNS) disorders, closed head injury with greater than 30 min loss of consciousness, open head injury of any kind, schizophrenia, seizure disorder, a sole *DSM-IV* diagnosis of alcohol use disorder, or current neuroleptic treatment were excluded from participation. The overall sample was 85% African American.

Among our 239 participants, 141 were seronegative for both HIV and HCV (Group HIV− HCV−), 49 were monoinfected with HIV (HIV+) and 30 with HCV (HCV+), and 19 were dually infected (HIV+ HCV+). HIV and HCV serostatus were EIA verified for all participants; 85% of the HIV+ participants were prescribed combination antiretroviral therapy (cART). Forty-six percent of the participants' HIV RNA levels (viral loads) were undetectable with a lower limit of 40. Median CD4 lymphocyte counts at testing were 382 (Interquartile range [IQR] 200, 605) and median nadir CD4 counts were 163 (IQR 29, 260). Current and nadir CD4 counts for the HIV+ compared with HIV+ HCV+ groups did not differ significantly (Current: $\chi^2(1) = 2.28$, $p = .13$; Nadir: $\chi^2(1) = 2.67$, $p = .10$). Viral loads were undetectable for 49% of the HIV+ and 37% of the HIV+ HCV+ groups, $\chi^2(1) = -.81$, $p = .37$. None of the HCV+ participants had received interferon or other antiviral therapy.

Procedure

Tests administered were part of a larger study protocol administered over two 120–150 min visits to the Psychiatric Institute at the University of Illinois at Chicago. Bachelor's level research assistants under the supervision of a board-certified neuropsychologist (EMM) conducted testing. Written informed consent was obtained on arrival for the first study visit. On both study visits, the participants underwent a breathalyzer test and provided a urine sample for on-site rapid toxicology screen for cocaine, cannabis, opioids, and methamphetamines (DrugCheck NxStep #61020) to ensure abstinence from drugs and alcohol at the time of testing. If a potential participant tested positive for cocaine, opioids, or methamphetamine, the visit was terminated, the participant received no payment, and the visit was rescheduled.[2] All participants were informed of these contingencies before the testing visit. They received $45 cash compensation for their time and transportation costs at the completion of each study visit.

Measures

Clinical and personality measures. Subjects were administered the Wechsler Test of Adult Reading (Wechsler, 2001) to estimate premorbid Full Scale IQ, and a series of paper and pencil measures of potentially confounding conditions comorbid with substance use disorders (SUDs). Measures of comorbid conditions included the Post Traumatic Stress Disorder (PTSD) Check List-Civilian Version (Blake et al., 1995); the Wender Utah Rating Scale (WURS; Stein et al., 1995) for symptoms of Attention Deficit Disorder (ADD); the Levenson Self-Report Psychopathy Scale to index antisocial tendencies (Levenson, Kiehl, & Fitzpatrick, 1995); the Sensation Seeking Scale-V (Zuckerman, 1996); and the Beck Depression Inventory-II (Beck, Steer, Ball, & Ranieri, 1996). These measures were administered to determine comparability of study groups and for use as potential covariates.

Substance use. All participants were administered the SCID-SAM (First et al., 1997) to determine if they met criteria for current or previous substance use disorders; the Addictions Severity Index (McLellan, Luborsky, Woody, & O'Brien, 1980); and the

[1] Following established procedures in the published neuroAIDS literature, participants who tested positive for tetrahydrocannabinol (THC) were not excluded if the toxicology screen was negative for all other substances. THC metabolites can be detected in urine for up to 25 days postingestion (Verstraete, 2004). However, participants were not informed of this single exception.

[2] A positive test for THC was not grounds for exclusion.

Kreek-McHugh-Schluger-Kellogg scale (Kellogg et al., 2003), used as a proxy of severity of alcohol, cocaine, and opioid dependence based on the participant's estimate of the amount of money spent, time duration, and frequency of use at the time of their heaviest use of each substance.

Delay discounting. All subjects completed the Monetary Choice Questionnaire (MCQ; Kirby, Petry, & Bickel, 1999), a 27-item paper and pencil measure frequently used in studies of impulsive choice. Each MCQ item queries the subject's preference for a small monetary reward available immediately or a larger reward available after a time delay ranging from 7 to 186 days (e.g., "would you prefer $5 now or $10 one week from now?") Both magnitude of reward and delay are varied across items. The dependent variable is *k,* the rate at which an individual discounts rewards, that is computed using Mazur's hyperbolic discounting function (Mazur, 1987):

$$V_d = A/(1 + k)D$$

where V_d is the present value of a delayed reward, A is the value of the delayed reward, D is the length of the delay interval, and k indexes the degree of delay discounting. Higher k values indicate a higher rate of discounting (i.e., a more rapid decline in perceived reward value as time delay increases).

Statistical Analyses

Demographic, substance use, and comorbidity data were compared using one-way analyses of variance (ANOVA) for parametric data, Kruskal-Wallis and Mann–Whitney U tests with the z approximation for nonnormally distributed data, and χ^2 tests for categorical data. A p value of .05 was used for all group comparisons. Bonferroni-corrected t tests were used for post hoc comparisons. Delay discounting k coefficients were analyzed using HIV × HCV factorial analysis of variance (ANOVA).

Results

Group Characteristics

Table 1 shows demographic, substance use, and comorbid characteristics for the four participant groups. Groups were well matched overall on demographic variables, except that HCV+ and HIV+ HCV+ groups were significantly older than HIV+ and HIV− HCV− groups, omnibus $F(3, 235) = 12.78$, $p < .001$; Bonferroni-corrected comparisons: HIV− HCV− versus HCV+, mean difference = −7.69, $p < .0001$; HIV− HCV− versus HIV+ HCV+, mean difference = −4.81, $p = .03$; HIV+ versus HCV+, mean difference = −8.30, $p < .001$; HIV+ versus HIV+ HCV+, mean difference = −5.42, $p = .03$. There were no significant group differences in mean years of education, estimated Full Scale IQ, or distribution by sex or race, $p > .11$ for each test.

Comorbid Disorders

The four groups were also well matched on comorbid characteristics. There was a significant group difference in Beck Depression Inventory-II (BDI-II) scores $F(3, 235) = 4.94$, $p = .002$. Post hoc tests revealed that the HIV+ group had higher BDI-II scores than the HIV− HCV− group (mean difference = −5.27, $p = .002$); No significant group differences were detected on measures of sensation seeking, ADD symptoms, or antisocial behavior, $p > .14$ for each test. The omnibus F value for mean PCLC scores was significant, $F(3, 235) = 3.57$, $p = .03$, but post hoc comparisons yielded no significant mean differences among the four groups (all p values ≥ .09).

Substance Use Characteristics

There were no significant overall group differences in mean ASI Alcohol composite scores, $p > .05$. The omnibus F statistic for mean ASI Drug scores was significant, $F(3, 235) = 2.87$, $p = .04$, but Bonferroni-corrected post hoc comparisons yielded no significant mean differences among the four groups, $p \geq .10$ for all tests. As expected[3], injection drug use (IDU) and opioid dependence were significantly more prevalent, and years of heroin use were significantly higher, among the HCV+ and HIV+ HCV+ groups compared with HIV− HCV− and HIV+ groups, IDU: $\chi^2(3) = 87.8$, $p < .0001$; Opioid dependence: $\chi^2(3) = 28.8$, $p < .0001$; Years used: $\chi^2(3)$ 19,2, $p < .0001$. The HIV− HCV−, HCV+ and HIV+ HCV+ groups had all used heroin significantly more recently and scored significantly higher on the KMSK-Heroin subscale compared with the HIV+ group, days since last heroin use: $\chi^2(3) = 11.54$, $p < .01$; KMSK-Heroin: $F(3, 235) = 9.47$, $p < .001$; $p < .005$ for each comparison. Prevalence of cocaine dependence was significantly higher among the HIV+ compared with the HCV+ groups, $\chi^2(3) = 8.63$, $p = .04$; and the HIV− HCV− group had used cocaine for significantly fewer years compared with the HIV+ HCV+ group, $\chi^2(3) = 8.63$, $p = .03$. There were no statistically significant group differences on any measure of alcohol misuse, including prevalence of *DSM–IV* diagnoses, years of use, mean KMSK-Alcohol scores, or number of days since last use, $p > .05$ for all tests. Approximately 10% of each group tested positive for tetrahydrocannabinol (THC) on urine toxicology screening, $\chi^2(3) = .08$, $p = .99$.

Delay Discounting

k values were nonnormally distributed and were consequently natural log-transformed. There were no significant correlations between transformed k values and any demographic, substance use, or comorbidity variables, so no covariates were added to the analyses.

HIV and HCV serostatus. Figure 1 shows discounting rates for all subject groups. Analysis of transformed k coefficients showed a significant main effect for HCV serostatus, $F(1, 235) = 7.97$, $p = .005$, $d = -.46$, and inspection of the means indicated that HCV-seropositive groups discounted at significantly higher rates compared with HCV-seronegative groups. There was no significant main effect for HIV serostatus, $F(1, 235) = 1.62$, $p = .20$, $d = .18$, and the HIV × HCV interaction was nonsignificant, $F(1, 235) = .06$, $p = .80$, $\eta_p^2 = .001$.

Among the HIV+ participants, there were no group differences in mean k coefficients for participants with and without a current or lifetime diagnosis of immunologic AIDS (i.e., current or nadir

[3] HCV is transmitted significantly more efficiently through blood-borne contact, primarily through injection drug use, than by unprotected sex (Terrault et al., 2013).

Table 1
Demographic, Substance Abuse, and Comorbidity Characteristics by HIV and HCV Serostatus

	HIV− HCV− (*N* = *141*)	HIV+ (*N* = 49)	HCV+ (*N* = 30)	HIV+ HCV+ (*N* = *19*)	Statistic	*p*
Demographic						
Age (years)[a]	41.5 (7.6)	40.9 (5.6)	49.2 (6.1)	46.3 (6.8)	12.8	.0001
Education (years)[a]	11.6 (1.4)	11.9 (2.2)	12.1 (1.6)	11.4 (2.3)	1.0	.41
Estimated FSIQ[b]	87.5 (8.5)	90.4 (10.9)	88.6 (9.3)	84.9 (9.3)	2.0	.11
% Female	30	35	20	26	2.0	.56
% African American	84	86	83	83	1.8	.94
Substance use						
Addiction Severity Index[a]						
Alcohol	.15 (.09)	.13 (.09)	.15 (.16)	.16 (.09)	0.5	.71
Drug	.08 (.04)	.08 (.05)	.10 (.06)	.10 (.06)	2.9	.04
KMSK scores[a]						
Alcohol	10.0 (2.8)	10.1 (2.4)	10.3 (2.6)	9.7 (4.1)	0.2	.91
Cocaine	12.6 (3.6)	13.3 (2.7)	11.8 (5.1)	13.5 (4.2)	1.3	.27
Heroin	5.6 (.44)	2.1 (.60)	7.6 (.99)	7.1 (1.24)	9.5	.0001
% *DSM-IV* dependence						
Alcohol	62	74	63	74	2.6	.46
Cannabis	62	55	70	63	1.8	.61
Cocaine	84	94	70	86	8.6	.04
Opioids	57	26	83	74	28.8	.0001
Years used[c]						
Alcohol	20 (10, 25)	17 (11, 28)	21 (15, 35)	25 (5, 30)	6.2	.10
Cannabis	10 (4, 20)	13 (4, 22)	14 (6, 22)	15 (4, 22)	2.7	.45
Cocaine	12 (4, 20)	16 (9, 19)	17 (10, 26)	18 (15, 20)	9.1	.03
Heroin	10 (5, 19)	8 (4, 15)	20 (6, 30)	25 (20, 30)	19.2	.0001
Days since last use[c]						
Alcohol	120 (60, 365)	203 (124, 502)	160 (60, 330)	195 (78, 1825)	2.4	.48
Cannabis	1095 (131, 5840)	547 (112, 5909)	730 (179, 9125)	4380 (195, 10585)	3.7	.30
Cocaine	137 (65, 301)	203 (124, 341)	120 (51, 199)	113 (62, 195)	0.8	.85
Heroin	130 (78, 240)	330 (153, 1505)	120 (51, 199)	179 (75, 3650)	11.5	.009
% Injection drug use	11	12	73	79	87.8	.0001
% Overdose	24	18	33	42	5.4	.15
Comorbidities[a]						
SSS-V	14.6 (6.5)	15.7 (6.2)	15.5 (5.5)	15.0 (6.8)	0.5	.680
PCL-C	35.4 (11.1)	40.6 (16.8)	41.8 (14.0)	34.6 (11.7)	3.6	.020
WURS	40.0 (17.5)	38.9 (21.5)	34.0 (22.0)	30.0 (19.6)	1.8	.150
SRPS	51.9 (10.2)	52.8 (9.9)	49.4 (9.8)	56.1 (9.5)	1.9	.140
BDI-II	10.0 (8.2)	15.3 (10.1)	13.1 (9.3)	10.3 (7.3)	4.9	.002

Note. *DSM-IV* = Diagnostic and Statistical Manual for Mental Disorders-Fourth Edition; FSIQ= full-scale IQ; HCV = hepatitis C virus; KMSK = Kellogg-McHugh-Schluger-Kreek Scale; SSS-V = Sensation Seeking Scale-V; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian Version; WURS = Wender Utah Rating Scale; SRPS = Self-Report Psychopathy Scale; BDI-II = Beck Depression Inventory-II.
[a] Means and *SD*s. [b] Estimated by Wechsler Test of Adult Reading. [c] Medians, interquartile ranges.

CD4 < 200), current: $F(1, 66) = .057$, $p = .81$; lifetime: $F(1, 54) = 2.52$, $p = .12$; or undetectable viral load, $F(1, 66) = .001$, $p = .90$.

Substance use effects. Discounting rates did not differ significantly among participants with and without a positive toxicology screen for THC, $F(1, 237) = 2.38$, $p = .12$; *DSM–IV* diagnosis of opioid or cocaine dependence, opioid dependence, $F(1, 237) = .74$, $p = .39$; cocaine dependence, $F(1, 237) = .84$, $p = .36$; or opioid substitution treatment, $F(1, 138) = 1.44$, $p = .23$. Given the significantly higher prevalence of IDU among the HCV+ participants, we conducted a two-way HCV × IDU ANOVA with the HIV+ participants excluded, to address the possibility that increased discounting rates could be attributed more readily to IDU history. This analysis revealed a significant main effect for HCV serostatus, $F(1, 66) = 4.87$, $p = .03$, Cohen's $d = -.60$, but the main effect for IDU and the HCV × IDU interaction were not statistically significant, IDU history, $F(1, 66) = .20$, $p = .66$, Cohen's $d = .06$; HCV × IDU $F(1, 66) = .07$, $p = .80$, $\eta_p^2 = .001$. Additionally, we compared *k* coefficients among heroin users with and without an IDU history (i.e., inhaled or smoked heroin). There were no significant differences in delay discounting according to route of administration, $F(1, 138) = 2.27$, $p = .13$.

In light of Meade and colleagues' report of higher discounting rates among HIV+ subjects with recent, but not past, cocaine use, we compared *k* values between HIV+ and HIV− participants who had used cocaine within the past 6 months with HIV+ and HIV− SDIs who used cocaine more than 6 months before testing.[4] We found a significant main effect for recent cocaine use, $F(1, 226) = 5.33$, $p = .02$, Cohen's $d = -.33$, but not for HIV serostatus, $F(1, 226) = 2.34$, $p = .13$, $d = .22$, or for the HIV Serostatus × Recent Cocaine interaction, $F(1, 226) = 2.97$, $p = .13$, $\eta_p^2 = .01$. We conducted a similar comparison of *k* values between HIV+ and

[4] Only 4% of subjects reported no cocaine use, so sample size was insufficient for a nonusing control group

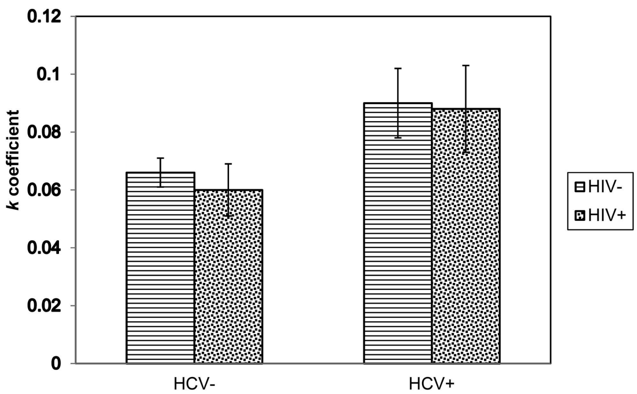

Figure 1. Mean natural log-transformed *k* coefficients for uninfected, monoinfected with HIV or hepatitis C virus (HCV), or coinfected groups.

HIV− participants with and without reported use of cannabis within the past 6 months. There were no significant main effects for recent cannabis use, $F(1, 219) = 1.01$, $p = .48$, or HIV serostatus, $F(1, 219) = 1.01$; $p = .32$; and the HIV Serostatus × Recent Cannabis interaction did not reach statistical significance, $F(1, 219) = 2.16$, $p = .14$. Finally, there were no significant correlations between *k* coefficients and number of days since last use of alcohol ($r = .04$), cannabis ($r = .10$), cocaine ($r = -.05$), or heroin ($r = -.04$; all $ps > .14$)

Delay discounting and risk behavior. Injections at bodily sites such as the groin or neck are much more dangerous than those at the antecubital fossa: these regions are more difficult for the user to see and contain larger veins, increasing the risk of overdose, infection, and venous damage (Darke, Ross, & Kaye, 2001). We speculated that riskier injection practices might be associated with higher discounting rates. On interview, all study participants who endorsed any injection history, regardless of serostatus, were asked if they had injected at each of seven body sites (e.g., antecubital fossa, foot, hand, neck) using categories used by Darke and colleagues (2001) in a large interview study of Australian injecting drug users. We found a significant positive correlation between *k* values and total number of injection sites, Spearman's rho = .32, $p = .01$ ($n = 58$).

Finally, we conducted multiple regression analyses to investigate if HCV and total injection sites independently predicted delay discounting rates ($n = 61$). Using forward multiple regression we entered HCV serostatus followed by injection sites, with *k* as the dependent variable. Both HCV serostatus and number of injection sites contributed significant predictive variance (HCV: $\beta = .246$, $p = .04$; Injection sites: $\beta = .256$, $p = .05$).

Discussion

In the current study, we investigated potential effects of HIV and HCV serostatus on delay discounting, a tendency to overvalue immediate over delayed rewards that is broadly characteristic of addictive disorders, among 239 SDIs. The groups were well matched on demographic and comorbid variables, with the exception that both HCV+ groups were significantly older than the HCV− groups. Subjects were verified abstinent from drugs and alcohol at testing.[5]

We found no evidence that delay discounting, as indexed by *k* coefficients, differed significantly among HIV+ compared with HIV− SDIs. Additionally, delay discounting was not associated with HIV disease severity. *K* values did not vary significantly according to severity of immunosuppression (CD4 counts) or level of HIV RNA (viral load).

By contrast, we found a significant association between a positive HCV serostatus and increased discounting rates. Compared with the HIV−infected participants, individuals seropositive for HCV were significantly older with a higher prevalence of opioid dependence. However, current evidence supports no effects of older age on delay discounting (Green, Myerson, & Ostaszewski, 1999), and discounting rates did not differ significantly among study participants with and without a history of opioid dependence, which argue against attributing the current finding to nonspecific effects of heroin addiction or aging. Finally, although our study did not obtain indices of HCV disease severity (e.g., indicators of fibrosis) there is no published evidence that discounting rates are elevated nonspecifically by liver disease.

A history of IDU was significantly more common among the HCV+ SDIs, consistent with HCVs much greater transmission efficiency by blood borne than sexual contact, raising the question if the HCV+ participants' increased discounting rates were more readily attributable to IDU history. We found no significant differences in discounting rates among all participants with and without a history of IDU. In a follow-up analysis excluding HIV+ participants, the statistically significant main effect for HCV serostatus was unchanged, with a medium effect size (Cohen's *d*) of .60, whereas the main effect for IDU history and HCV × IDU interaction did not reach statistical significance. Our results provide strong evidence of a relationship between HCV serostatus and discounting, but the nonsignificant effects for IDU should be interpreted with some caution. Only 26% of the HCV-monoinfected group was IDU−, raising the possibility that that these comparisons were underpowered and precluding a conclusion that HCV serostatus is more strongly associated with delay discounting than IDU. However, it is clear that increased delay discounting among our subjects could be attributed to in part to HCV serostatus independent of injection drug history. In this regard, Huckans and colleagues previously reported that HCV+ individuals showed elevated discounting rates regardless of substance use history (Huckans et al., 2011).

We found no evidence of additive or interactive effects of HIV and HCV serostatus on discounting rates, as mean *k* coefficients did not differ significantly between HCV+ participants with or without HIV coinfection. This finding may appear somewhat atypical, because neurocognitive impairment is typically more common and severe among coinfected compared with monoinfected individuals (Cherner et al., 2005; Martin, Novak et al., 2004); however, there are no defined cutoff scores for the MCQ, suggesting that discounting rates are not readily classifiable as "impaired" or "unimpaired."

Several candidate neural and cognitive mechanisms may have contributed to the pattern of results. Both HIV and HCV are detectable in brain (Laskus et al., 2005) and associated with

[5] With the single exception of THC-positive toxicology screens for ∼10% of each group.

abnormal cerebral metabolites in frontal white matter and basal ganglia on MR spectroscopy (Forton et al., 2005), but at least one study using positron emission tomography (PET) scanning has also reported abnormal glucose metabolism in limbic association cortex among HCV+ individuals (Heeren et al., 2011); see also (Letendre et al., 2007). This finding has potential relevance to the current discussion since both insula and ventral (limbic) striatum are activated during delay discounting (Wittmann, Leland, & Paulus, 2007), but the possibility that limbic mechanisms might contribute to increased discounting rates among HCV+ remains speculative pending more detailed neuroimaging and neuropathological investigations.

Findings from our previous studies of decision making using the Iowa Gambling Task (IGT; Gonzalez et al., 2005; Martin, Pitrak et al., 2004) may shed light on the absence of higher discounting rates among HIV+ compared with HIV− SDIs. Although cognitive and neural mechanisms of discounting and IGT performance are not identical, each task engages processing of immediate and delayed rewards, either explicitly (delay discounting), or implicitly (IGT). The IGT requires the capacity to forego large immediate wins when smaller wins will result in a winning score in future. The IGT measures decision making *under ambiguity*: No information is provided to guide subjects' choices, so successful performance requires the capacity to deduce the optimal strategy through feedback and over trials. By contrast, delay discounting engages decision making *under specified risk*, providing specific item by item information on the tradeoff between reward size and time delay to guide subjects' choices. We (Martin et al., 2013) recently reported that HIV+ SDIs perform the IGT consistently more poorly compared with HIV− SDIs, but performed similarly on the Cups Task (Weller, Levin, & Bechara, 2010), a multiple trial two-choice measure of decision making under risk. We speculated that HIV+ SDIs made poorer decisions only when given no explicit information to guide response selection, suggesting that implicit learning deficits might contribute to their poor performance of the IGT. This hypothesis is compatible with the current findings and suggests that other potentially noncognitive mechanisms (e.g., responsivity to reward) may drive increased discounting among HCV+ individuals.

Finally, our preliminary finding of higher discounting rates among participants who reported more dangerous injection practices suggests that a trait-like tendency to overvalue immediate rewards would predispose some SDIs toward greater willingness to engage in highly risky injection practices and future studies should investigate if discounting rates are also elevated among individuals practicing risky sex.

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