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## Reward, Attention, and HIV-related Risk in HIV+ Individuals

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### Abstract

Human immunodeficiency virus (HIV) is often contracted through engaging in risky reward-motivated behaviors such as needle sharing and unprotected sex. Understanding the factors that make an individual more vulnerable to succumbing to the temptation to engage in these risky behaviors is important to limiting the spread of HIV. One potential source of this vulnerability concerns the degree to which an individual is able to resist paying attention to irrelevant reward information. In the present study, we examine this possible link by characterizing individual differences in value-based attentional bias in a sample of HIV+ individuals with varying histories of risk-taking behavior. Participants learned associations between experimental stimuli and monetary reward outcome. The degree of attentional bias for these reward-associated stimuli, reflected in their ability to capture attention when presented as task-irrelevant distractors, was then assessed both immediately and six months following reward learning. Value-driven attentional capture was related to substance abuse history and non-planning impulsiveness during the time leading up to contraction of HIV as measured via self report. These findings suggest a link between the ability to ignore reward-associated information and prior HIV-related risk-taking behavior. Additionally, particular aspects of HIV-associated neurocognitive disorders were related to attentional bias, including motor deficits commonly associated with HIV-induced damage to the basal ganglia.

### Keywords

attention; reward; learning; HIV; HIV-associated neurocognitive disorders (HAND); risky behavior; impulsiveness; substance abuse; basal ganglia; dopamine; addiction

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Human immunodeficiency virus (HIV) is a serious health condition affecting an estimated 1.2 million people in the United States (Centers for Disease Control and Prevention, 2014), and 35 million people worldwide (World Health Organization, 2014). Transmission of HIV occurs through the exchange of bodily fluids, typically via unprotected sex and the sharing of needles used to administer drugs of abuse (Centers for Disease Control and Prevention, 2015). Therefore, one key to preventing the spread of HIV is reducing the degree to which individuals engage in these high-risk behaviors. Prevention efforts in this area have largely focused on education, routine HIV testing, and the provision of materials such as condoms and clean needles (e.g., World Health Organization, 2014). This approach, however, ignores the underlying factors that motivate an individual to engage in HIV-risk behaviors. One potential reason why reducing engagement in these risky behaviors is so challenging is that they have a high degree of incentive salience (Berridge, 2012; Berridge & Robinson, 1998). That is, HIV-risk behaviors are associated with a reward value, creating a powerful motivation to engage in these behaviors when opportunities to do so are encountered. For certain individuals, the strength of this incentive salience may overpower the goal of abstaining from HIV-risk behaviors. Understanding the cognitive processes that contribute to this reward-driven component of HIV-associated risk could lead to insights into how to more effectively target prevention efforts, as well as provide a means of more accurately identifying high-risk individuals who might especially benefit from these efforts.

There is considerable evidence that attention is strongly influenced by reward information (e.g., Anderson, Laurent, & Yantis, 2011a, 2011b; Hickey, Theeuwes, & Chelazzi, 2010). Our ability to process sensory information is capacity-limited, and attention selects which among multiple competing sources of information receive representation (Desimone & Duncan, 1995). Once a stimulus has been learned to predict a reward, a persistent tendency to preferentially attend to that stimulus develops (Della Libera & Chelazzi, 2009; Peck, Jangraw, Suzuki, Efem, & Gottlieb, 2009; Raymond & O'Brien, 2009; Serences, 2008). Importantly, a bias to attend to previously reward-predicting stimuli is evident even when such stimuli are inconspicuous and task-irrelevant, indicating that reward history plays a distinct role in the guidance of attention (Anderson et al., 2011a, 2011b, 2014; Anderson & Yantis, 2012). We refer to this consequence of reward learning on information processing as *value-driven attention* (see Anderson, 2013, for a review).

Evidence that attentional processes might contribute to the likelihood of engaging in risky reward-motivated behavior can be found in studies of addiction-related attentional biases. Substance abusers involuntarily orient attention toward stimuli that are associated with their substance of abuse, whereas individuals with no history of substance abuse do not show such selection biases (Field & Cox, 2008; Lubman, Peters, Mogg, Bradley, & Deakin, 2000; Mogg, Bradley, Field, & De Houwer, 2003; Stromark, Field, Hugdahl, & Horowitz, 1997). Patients who show the largest attentional biases for drug-related stimuli are the most likely to relapse during the course of treatment (Carpenter, Schreiber, Church, & McDowell, 2006; Marissen et al., 2006), suggesting a relationship between such attentional biases and the choice to consume an abused substance in spite of the conflicting goal of abstinence.

Recent evidence from our lab suggests that drug-related attentional biases in addiction might reflect a more general sensitivity to reward's influence on attention that extends beyond drug reward per se. In that study, opioid-dependent and control participants first learned associations between color stimuli and monetary reward during a training phase. These reward-associated stimuli then served as non-target distractors during a subsequent test phase. The results showed substantially greater attentional capture by the previously reward-associated stimuli in the opioid-dependent group (Anderson, Faulkner, Rilee, Yantis, & Marvel, 2013). This effect was similar to the differential attentional processing attributed to drug cues (e.g., Carpenter et al., 2006; Field & Cox, 2008; Lubman et al., 2000; Marissen et al., 2006) except in our study, the stimuli were "drug neutral", consisting of colors associated with monetary reward. This finding suggests the possibility that susceptibility to value-driven attentional capture, as a broad cognitive trait, might play a role in problematic reward-approach behaviors. In further support of this, value-driven attentional biases for arbitrary reward-associated stimuli are also especially prominent in adolescence (Roper, Vecera, & Vaidya, 2014), a period of life marked by increases in risk-taking behavior and disproportionately high incidences of new HIV infection (Centers for Disease Control and Prevention, 2015).

Certain aspects of value-driven attention suggest that it might also be related to HIV-associated neurocognitive disorders (HAND). The value-driven orienting of attention is mediated by priority signals within the dopamine-rich basal ganglia (Anderson, Laurent, & Yantis, 2014; Gottlieb, Hayhoe, Hikosaka, & Rangel, 2014; Yamamoto, Kim, & Hikosaka, 2013; see also Nickolaou, Field, Critchley, & Duka, 2013), a region of the brain strongly affected by HIV and linked to associated motor control symptoms (Aylward et al., 1993; Berger, Kumar, Kumar, Fernandez, & Levin, 1994; Dal Pan et al., 1992; Navia, Cho, Petito, & Price, 1986; Sardar, Czudek, & Reynolds, 1996). In addition, individuals with lower visual working memory capacities are especially prone to attentional capture (Fukuda & Vogel, 2009), including attentional capture by reward-associated stimuli (Anderson et al., 2011b, 2013; Anderson & Yantis, 2012), which is thought to reflect difficulty exerting goal-directed control over information processing. Both working memory (e.g., Caldwell et al., 2014; Chang et al., 2001; Woods et al., 2010) and motor (e.g., Reger, Welsh, Razani, Martin, & Boone, 2002; Arendt, Hefter, Elsing, Strohmeier, & Freund, 1990) impairments have been linked to HAND. Although the advent of highly active antiretroviral therapy (HAART) has seen a reduction in the severity of HAND (e.g., Sacktor, Skolasky, Lyles, Esposito, Selnes, & McArthur, 2000; Sacktor et al., 2001; Suarez et al., 2001), basal ganglia atrophy (Becker et al., 2011) and cognitive and motor impairments (e.g., Sacktor et al., 2002; Simioni et al., 2010) are still evident in HAART-treated patients. It is therefore possible that the consequences of HIV can further predispose an individual to be influenced by reward information, posing an additional risk factor for future decision-making. As HAND can become more severe with increased cerebrospinal fluid and brain viral load (e.g., Ellis et al., 2002; McArthur et al., 1997), managing risk-taking behavior post contraction of HIV reflects an important treatment goal.

The development of attentional biases for reward stimuli has not been studied in the context of HIV-risk or HAND, nor has it been linked to substance abuse in individuals who are not currently substance dependent. Therefore, in the present study, we examined the potential

link between value-driven attention and (1) impulsive behaviors that place an individual at risk of acquiring HIV and (2) working memory and motor dimensions of HAND. Because HIV can be acquired as a result of a range of underlying risk-taking tendencies, from a single risky decision or as the result of a serial pattern of risky behavior, we took an individual differences approach to this question.

HIV+ patients first learned to associate experimental stimuli with monetary reward in a training phase. In a subsequent test phase we measured attentional biases for these reward-associated stimuli when presented as irrelevant distractors. In general, when presented with such a distractor, people take longer to visually locate a target; this increase in response time (RT) represents the degree of value-driven attentional capture (e.g., Anderson, 2013; Anderson et al., 2011b, 2013). As this bias to be drawn towards previously reward-associated stimuli has been shown to persist for up to nine months without further training in healthy college-age individuals (Anderson & Yantis, 2013), we also had participants in the present study return and complete the test phase again during a second visit six months later. We related inter-individual differences in the magnitude of this bias to measures of risk-taking history: prior substance dependence and impulsive behaviors during the period leading up to HIV+ diagnosis, in addition to measures of visual working memory capacity and motor control. We hypothesized significant relationships among these variables, consistent with the idea that how reward information is processed by the attention system is related to the high-risk behaviors that contribute to the spread of HIV and become more severe with reduced cognitive and motor abilities related to HAND.

## Material and Methods

### Participants

Twenty-four HIV+ patients (age 38–68 years, mean = 56 years, 5 females) were recruited from referrals to the HIV Neurology Service at Johns Hopkins Hospital. The patients were treated for HIV with a daily schedule of antiretroviral medications (e.g., Epzicom, Reyataz, Truvada). Each patient had a unique medication prescription and schedule. Patients had been diagnosed as HIV+ for an average of 19.0 years (range = 2–36 years). Patients self-reported maintaining an average adherence of 91.7% percent (range = 72–99%) to their antiretroviral medications since being diagnosed with HIV. Clinical data, including HAND stage (Antinori et al., 2007) and Karnofsky performance status (Karnofsky & Burchenal, 1949), were tracked by the fourth author's research team as a part of an ongoing investigation and were made available. The Karnofsky performance status provides a measure of global functioning that reflects the degree to which the individual experiences difficulty performing the tasks of everyday life, with lower scores indicating greater impairment.

A detailed history of lifetime drug and alcohol exposure was obtained during the first visit using a modified version of the Lifetime Drug Use Questionnaire (LDU; Czermak et al., 2005; Marvel, Faulkner, Strain, Mintzer, & Desmond, 2012), and then updated during the second visit. Six patients were cigarette smokers at the time of study. Patients tested negative for cocaine, amphetamine, methamphetamine, marijuana, opiates, phencyclidine, barbiturates, and benzodiazepines. This was confirmed by urine drug testing conducted on each day of testing (Aim Screen MultiDrug 9 by Germaine Laboratories). All participants

completed a brief version of the *Structured Clinical Interview for DSM-IV Axis I Disorders: Clinical Version (SCID-CV)*; First, Spitzer, Gibbon, & Williams, 1996) to screen for psychotic disorders and confirm substance dependence. Additional exclusionary criteria included a history of neurologic or major medical disorder (e.g., stroke, seizures, Parkinson's, etc.), serious head injury resulting in a loss of consciousness for more than 5 minutes, hepatitis C status that required current medication, and use of prescription stimulants.

### **Apparatus**

Participants completed all components of the experiment in a small, well-lit room. Computer-based tasks were run on a Dell Optiplex 380 and displayed on a Dell E171FP monitor positioned at a viewing distance of approximately 50 cm. All tasks were programmed in Matlab using the Psychophysics Toolbox (Brainard, 1997).

### **Assessment of Impulsiveness**

Each participant completed the Barratt Impulsiveness Scale (BIS-11) (Patton, Stanford, & Barratt, 1995). We adapted the instructions such that participants were asked to answer based on how they remembered behaving the twelve months leading up to their diagnosis as HIV+ (i.e., a premorbid behavioral rating). We also asked participants to separately complete the unadapted version of the BIS-11, with reference to the recent past, for comparison.

### **Assessment of Depressive Symptom Severity**

Each participant completed the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977). The CES-D was administered at both study visits.

### **Visual Working Memory Task**

As in our prior study (Anderson et al., 2013), all participants completed a color change-detection task (Luck & Vogel, 1997). On each of 120 trials, a memory array was presented following a 500 ms fixation period and consisted of the presentation of 2, 4, or 6 colored squares ( $1.38^\circ \times 1.38^\circ$ ) on a grey background. The color of the squares were selected from red, green, yellow, blue, cyan, orange, black, purple, and brown on each trial without replacement; each square was separated by at least  $2.06^\circ$  center-to-center. The memory array was presented for 100 ms and was followed by a blank 900 ms retention interval. After the retention interval, a single colored square was presented in a position previously occupied by a square in the memory array. This probe square was either the same or different in color as the square that had been previously presented in its location (equally-often). When the probe square was different in color, it was presented in a color not seen in the preceding memory array. Participants indicated whether they thought the color of the probed square had changed via a two alternative forced-choice key press, pressing standard keyboard letter "m" for reporting a change and "z" for reporting no change. The task was performed without time pressure. No feedback was provided during the task; participants completed 24 practice trials, randomly generated using the aforementioned parameters, during which feedback concerning accuracy was provided to ensure understanding of task instruction.

## Digit Span

Each participant completed both the forward and backward measures of the WAIS-III Digit Span test (Wechsler, 1997).

## Finger Tapping

Each participant completed the *finger tapping test* of the Halstead-Reitan Battery (Broshek & Barth, 2000). Participants performed 5–10 trials for each hand, starting with the right. The task was completed for a hand when the total number of taps for each trial was within five digits across five consecutive trials, or a maximum of ten trials was performed. Finger taps were averaged over all completed trials for each hand for each participant. Each participant performed several practice taps prior to beginning the task for each hand.

## Attentional Capture Task

**Training phase**—The attentional capture task was exactly identical to that reported in Anderson et al. (2013). The training phase consisted of visual search for a target circle among five non-target circles (see Figure 1A). The target circle was unpredictably red or green. Participants reported the orientation of a bar contained within the target as either vertical or horizontal via a key press, with the “z” key for vertical and the “m” key for horizontal. Bars contained within the non-target circles were randomly oriented at 45° to the left or to the right.

Each visual search array was followed by feedback indicating monetary reward. If participants responded correctly on the trial, a small amount of money was added to a running total that participants were informed they would be paid at the completion of the experiment. Importantly, one of the two target colors would yield a comparatively high reward of 10¢ on 80% of the trials, and a comparatively low reward of 2¢ on the remaining 20% (high-reward target); for the other color target, these contingencies were reversed (low-reward target). If participants did not respond correctly, the feedback indicated that 0¢ had been earned. Red served as the high-reward color for half of the participants.

Each trial in the training phase consisted of a fixation display for 400, 500, or 600 ms (randomly determined), which was followed by the search array for either 1200 ms or until a response was made. A 250 ms 1000 Hz beep informed participants if they failed to execute a response during the 1200 ms deadline, and such trials were scored as errors. The search array was followed by a blank screen for 1000 ms, the reward feedback display for 1500 ms, and then by a blank 1000 ms inter-trial-interval (ITI). The background of the screen was black, the fixation cross and oriented bars were white, and the non-target circles were drawn from the colors orange, blue, cyan, white, pink, and yellow on each trial without replacement. The fixation cross was  $1.09^\circ \times 1.09^\circ$  and each circle was  $3.95^\circ \times 3.95^\circ$ , positioned in one of six locations along an imaginary circle with a radius of  $8.12^\circ$ .

The training phase consisted of 240 trials, half of which contained a red target and half of which contained a green target. These trials were broken into four blocks of 60 trials, with a mandatory 30 sec break between blocks. Each color target appeared in each location equally-often, and each color target contained a vertical and horizontal bar equally often.

The order of trials was randomized for each participant. The training phase was preceded by 40 practice trials, randomly generated using the aforementioned parameters.

**Test phase**—The test phase consisted of visual search for a unique shape, either a circle among diamonds or a diamond among circles (see Figure 1B). The color of the shapes was irrelevant to the task, and participants were informed of this. Importantly, one of the non-target shapes was occasionally rendered in the color of a formerly reward-predictive target. On 25% of the trials, one of the non-targets was green and on a different 25% of the trials, one of the non-targets was red; these red and green shapes constituted the valuable distractors. On the remaining 50% of the trials, none of the shapes were red or green (distractor-absent trials). The targets were never red or green.

Participants made the same judgment concerning the orientation of the bar contained within the target, indicating whether it was vertical or horizontal. Importantly, they were no longer provided a monetary reward for doing so. Feedback following the search array only informed participants if their prior response was correct or not, with a check mark for correct responses and an “X” for incorrect responses. Bars contained within the non-target shapes were again randomly oriented at 45° to the left or to the right.

Each trial consisted of a fixation display for 400, 500, or 600 ms (randomly determined), a search array for 1500 ms or until a response was made, a feedback display for 1000 ms, and a 500 ms blank ITI. The positions and size of the stimuli and the colors used were identical to the training phase, and a beep informed participants if a response was not made within 1500 ms. The target was equally-often a diamond among circles and a circle among diamonds, and the target shape and its location were unrelated to the presence, color, and position of the distractors. The test phase also consisted of 240 trials, randomly ordered and separated into four blocks, and was preceded by 28 practice (distractor-absent) trials randomly generated using the same parameters.

**Assessment of awareness**—Following the test phase, awareness of the reward value of targets during the training phase was assessed. Participants were asked to indicate whether they thought (a) “the red circle was usually worth more than the green” (b) “the green circle was usually worth more than the red” or (c) “the two circles were usually worth about the same”. Participants who answered (c) were subsequently informed that one color circle was in fact usually worth more than the other, and were asked to guess which color it was.

## Procedure

Participation involved two visits. On Visit 1, participants performed the visual working memory task, the digit span task, the finger tapping task, the CES-D, and the BIS-11 with reference to recent behavior, in addition to both the training phase and test phase of the attentional capture task and the subsequent assessment of awareness. Participants were also interviewed about their drug use history during Visit 1. During Visit 2, participants completed the BIS-11 with reference to their behavior leading up to HIV+ diagnosis, and completed the test phase of the attentional capture task a second time without retraining of the stimulus–reward associations. Drug use history was also updated since Visit 1 (i.e., the past 6 months).

## Data Analysis

For the attentional capture task, only RT on correct trials was considered in the analyses of RT. RTs exceeding 3 standard deviations of the mean of a given condition for a given participant were eliminated. RTs faster than 200 ms (< 1% of trials when excluding one participant for Visit 2, see below) were considered anticipations and were not analyzed. One participant had difficulty meeting the response deadline and could not initially perform at or above chance level in the first two blocks of the test phase for Visit 1; for this participant, these blocks were considered additional practice and were not analyzed (same procedures as Anderson et al. (2013)). Visit 2 data was unusable for another participant, who did not comply with task instruction, performing at chance while making many anticipatory responses; correspondingly, analyses on Visit 2 data focus on the remaining 23 participants. For between-participant comparisons involving awareness of the reward contingencies and substance dependence history, due to unequal sample sizes, equal variance was not assumed.

For the visual working memory task, accuracy was recorded and visual working memory capacity was calculated as the number of items remembered using a standard formula that accounts for the probability of guessing correctly (Cowen, 2001). Four participants performed at or below chance in the visual working memory task for set size 6, but performed accurately at set sizes 2 and 4; only data from set sizes 2 and 4 were considered for these participants (same procedure as Anderson et al. (2013)).

Impulsiveness was measured as the total score obtained on the BIS-11. Additionally, impulsiveness was broken down into the three sub-scales of the BIS-11 (attentional impulsiveness, motor impulsiveness, and non-planning impulsiveness). Digit span was determined by summing the forwards and backwards measures. Analyses of finger tapping focused on the measure produced by the dominant hand. History of substance dependence was determined during the LDU interview and based upon criteria of the SCID (First et al., 1997); 13 of the 24 participants were identified as having previously been substance dependent using these criteria (for lifetime substance use, see Table 1). For the purposes of data analysis, HAND stage was quantified as 1–4 for normal, Asymptomatic Neurocognitive Impairment (ANI), Mild Neurocognitive Disorder (MND), and HIV-Associated Dementia (HAD), respectively.

In assessing awareness of the stimulus–reward contingencies, participants who correctly answered (a) or (b) to the awareness question were scored as being aware of the relationship, and participants who answered (c) as unaware. For participants who answered (c), the guessing rate was obtained from their response to the follow-up forced-choice question.

## Results

### Effect of Reward on Attention

**Training phase**—Participants were neither faster,  $t(23) = 0.77$ ,  $p = 0.452$ , nor more accurate,  $t(23) = -0.61$ ,  $p = 0.528$ , to report a high-reward target (mean = 794 ms, 81.1%) than a low-reward target (mean = 803 ms, 82.4%), suggesting that participants searched for each of the two target colors with roughly equal priority, as is commonly observed in this paradigm (e.g., Anderson et al., 2011a, 2013; Anderson, Leal, Hall, Yassa, & Yantis, 2014).



Of primary interest was how the stimulus–reward associations experienced during training would influence attention in the test phase, when the same color stimuli were presented as task-irrelevant distractors, thereby providing a sensitive measure of involuntary attentional bias.

**Test phase, Visit 1**—An analysis of variance (ANOVA) on mean RT with distractor condition (absent, low-value, high-value) as a factor revealed a main effect,  $F(2,46) = 8.15$ ,  $p = 0.001$ ,  $\eta_p^2 = 0.262$  (Figure 2A). Planned comparisons revealed that participants were significantly slower to report the target on high-value distractor trials compared to both low-value distractor,  $t(23) = 3.00$ ,  $p = 0.006$ ,  $d = 0.61$ , and distractor-absent trials,  $t(23) = 3.87$ ,  $p = 0.001$ ,  $d = 0.79$ , indicating robust value-driven attentional capture. Accuracy did not differ among the three conditions,  $F(2,46) = 0.53$ ,  $p = 0.590$  (80.0%, 78.3%, and 79.3% across the absent, low-value, and high-value distractor conditions, respectively).

**Test phase, Visit 2**—Six months after the reward training, value-driven attentional capture was no longer evident at the group level. The same ANOVA on mean RT revealed no main effect of distractor condition,  $F(2,44) = 0.20$ ,  $p = 0.823$  (Figure 2B). However, as the following sections will demonstrate, there were substantial individual differences in attentional capture across participants, with some demonstrating a large negative capture score in which RT was facilitated by the high-value distractor, consistent with inhibition of the distractor. As before, accuracy did not differ among the three distractor conditions,  $F(2,44) = 0.09$ ,  $p = 0.912$  (80.9%, 80.6%, and 81.1% across the absent, low-value, and high-value distractor conditions, respectively).

### Predicting Attentional Bias from Individual Difference Measures

We defined value-driven attentional capture as the slowing in RT caused by one's inability to ignore a high-value distractor relative to one's RT when no distractor was present, as we have done in prior studies (Anderson et al., 2011b, 2013; Anderson, Leal, et al., 2014; Anderson & Yantis, 2012). Here we examine factors that predict value-driven attentional capture in the present sample. All of the reported relationships remain significant if current smoking status is entered as a covariate.

**Relating attentional bias to prior risk-taking**—Self-reported impulsiveness in the twelve months leading up to HIV+ diagnosis was correlated with value-driven attentional capture both at Visit 1,  $r = 0.379$ ,  $p = 0.068$ , and at Visit 2,  $r = 0.444$ ,  $p = 0.034$ . Further analysis demonstrated that this relationship was restricted to the non-planning dimension of impulsiveness. At Visit 1, non-planning impulsiveness,  $r = 0.477$ ,  $p = 0.018$  (Figure 3A), but not attentional impulsiveness,  $r = 0.224$ ,  $p = 0.292$ , or motor impulsiveness,  $r = 0.189$ ,  $p = 0.377$ , was correlated with value-driven attentional capture. The same was true at Visit 2: non-planning:  $r = 0.536$ ,  $p = 0.008$  (Figure 3B); attentional:  $r = 0.192$ ,  $p = 0.379$ ; motor:  $r = 0.307$ ,  $p = 0.154$ . When entering all three impulsiveness dimensions into a simultaneous regression model to account for shared variance, only the non-planning dimension came out as significant at each of the two visits,  $\beta_s > 0.509$ ,  $p_s < 0.045$  (other dimensions:  $\beta_s < 0.134$ ,  $p_s > 0.596$ ). Similar but non-significant correlations were observed using the measure of current impulsiveness: total at Visit 1,  $r = 0.331$ ,  $p = 0.114$ , and at Visit 2,  $r = 0.376$ ,  $p =$

0.077; non-planning at Visit 1,  $r = 0.374$ ,  $p = 0.072$  ( $\beta = 0.366$ ,  $p = 0.134$ ), and at Visit 2,  $r = 0.341$ ,  $p = 0.111$  ( $\beta = 0.265$ ,  $p = 0.285$ ). Although correlated, only 50% of the variance in total impulsiveness and 42% of the variance in non-planning impulsiveness was shared between the two assessments (leading up to diagnosis and current), suggesting that each reflects unique variance attributed to the specific point in time queried. Participants were more impulsive leading up to diagnosis than at present: total  $t(23) = 2.21$ ,  $p = 0.037$ ,  $d = 0.45$  (mean difference = 4.6); non-planning  $t(23) = 2.28$ ,  $p = 0.032$ ,  $d = 0.47$  (mean difference = 2.4).

We additionally compared value-driven attentional capture between participants with and without a history of substance dependence. At Visit 1, value-driven attentional capture was higher for participants with a history of substance dependence (44 vs 14 ms),  $t(21.56) = 2.27$ ,  $p = 0.033$ ,  $d = 0.93$ . This difference was marginally significant at Visit 2 (11 vs -25 ms),  $t(20.92) = 2.07$ ,  $p = 0.051$ ,  $d = 0.87$ , with capture being *negative* for participants with no history of substance dependence,  $t(9) = -2.13$ ,  $p = 0.062$ ,  $d = 0.67$ .

### **Relating attentional bias to measures of cognitive and motor functioning—**

Finger-tapping performance was negatively correlated with value-driven attentional capture at both Visit 1,  $r = -0.479$ ,  $p = 0.018$  (Figure 4A), and Visit 2,  $r = -0.453$ ,  $p = 0.030$  (Figure 4B). Both of these correlations were impacted by an outlier, whose finger tapping performance differed from the group mean by more than 2.5 SD (3.1). The correlations remain significant if this participant's performance is set to 2.5 SD of the mean, but are not significant if the participant is entirely eliminated from the analysis. In replication of previous findings (Anderson et al., 2011b, 2013; Anderson & Yantis, 2012), value-driven attentional capture at Visit 1 was negatively correlated with visual working memory capacity,  $r = -0.366$ ,  $p = 0.040$  (one-tailed) (Figure 4C). This relationship was specific to the working memory capacity of the visual system, as no such relationship was observed between capture and digit span,  $r = -0.011$ ,  $p = 0.959$ . The relationship with visual working memory capacity was no longer evident at Visit 2,  $r = -0.154$ ,  $p = 0.242$  (one-tailed).

Twenty-nine percent of participants were classified as ANI, 42% as MND, and 21% as HAD at the time of study. HAND stage poorly predicted value-driven attentional capture, measures of impulsiveness leading up to HIV+ diagnosis, visual working memory capacity, and finger tapping ( $ps > 0.30$ ). The same was true of Karnofsky performance status ( $ps > 0.42$ ). Karnofsky scores ranged from 70–100 (mean = 90, SD = 10.7).

**Attentional bias, learning, and awareness—**During the post-experimental assessment of awareness, six participants correctly indicated the color that was associated with higher overall reward in the training phase, demonstrating explicit awareness of the relationship. The remaining 18 participants indicated that both colors were worth about the same (i.e., option C) and were scored as unaware. Of the participants who were unaware of the relationship between color and reward, their guessing rate was at chance (50%). Value-driven attentional capture did not differ between aware and unaware participants (33 vs 28 ms, respectively) during Visit 1,  $t(10.06) = 0.27$ ,  $p = 0.796$ ; however, this difference was significant at Visit 2 (-34 vs 6 ms),  $t(16.47) = -2.57$ ,  $p = 0.020$ ,  $d = 1.10$ , with capture being significantly *negative* for aware participants,  $t(5) = -3.24$ ,  $p = 0.023$ ,  $d = 1.32$ .

Although increased priority for the high-reward target during the training phase (faster RTs compared to low-reward target trials) was not evident at the group level, individual differences in this measure were significantly correlated with value-driven attentional capture at Visit 1,  $r = 0.448$ ,  $p = 0.028$ , demonstrating a close coupling between the influence of reward on performance across the two phases of the experiment. However, this relationship was no longer reliable during Visit 2,  $r = 0.219$ ,  $p = 0.315$ , suggesting that factors beyond the strength of the originally learned bias played a prominent role in how well a person retained information about the stimulus–reward associations six months later.

**Other measures**—Both at Visit 1 and Visit 2, value-driven attentional capture was not significantly correlated with age,  $r_s > -0.046$ ,  $p_s > 0.844$ , years of education,  $r_s > -0.256$ ,  $p_s > 0.228$ , or household income,  $r_s > -0.172$ ,  $p_s > 0.457$ . Neither was value-driven attentional capture significantly correlated with age of first illicit drug use,  $r_s > -0.329$ ,  $p_s > 0.136$ , or duration of abstinence from illicit drugs,  $r_s > -0.027$ ,  $p_s > 0.911$ . The severity of depressive symptoms as measured using the CES-D was not correlated with any of the dependent measures acquired in the present study ( $p_s > 0.128$ ), with the exception of current non-planning impulsiveness,  $r = 0.424$ ,  $p = 0.039$ , and (marginally) premorbid attentional impulsiveness,  $r = 0.350$ ,  $p = 0.094$  ( $p_s$  uncorrected for multiple comparisons). This suggests that our findings were not confounded by HIV-related depression. Further consistent with this, depressive symptoms have been shown to be *negatively* correlated with the magnitude of value-driven attentional capture in college students (Anderson, Leal, et al., 2014), which would only work against the reported relationships.

## Discussion

Our findings demonstrate that the degree to which an HIV+ individual is unable to resist paying attention to irrelevant reward information is correlated with the severity of impulsiveness leading up to HIV+ diagnosis and is greater for participants with a history of substance dependence. This suggests a link between value-driven attention and HIV-associated risk. In this regard, it is informative that the only dimension of impulsiveness that correlated with attentional capture was the non-planning dimension, which is the most directly related to risky decision-making. Years after substance dependence and other impulsive behaviors leading up to HIV+ diagnosis, an attentional correlate of these variables was still evident in our sample, suggesting that such sensitivity to the influence of reward information on the attention system reflects a persistent HIV-risk trait.

We additionally show that two neuropsychological factors related to HAND, working memory (e.g., Caldwell et al., 2014; Chang et al., 2001; Woods et al., 2010) and motor control (e.g., Reger et al., 2002; Arendt et al., 1990), are also related to susceptibility to value-driven attentional capture. Prior research has shown that the ability to exert control over attentional selection and thereby resist attentional capture is predicted by visual working memory capacity (Anderson et al., 2011b, 2013; Anderson & Yantis, 2012; Fukuda & Vogel, 2009). We show that, in HIV+ patients, the integrity of such capacity predicts susceptibility to value-driven attentional capture. No such relationship was evident using a measure of working memory capacity for non-visual information (WAIS-III digit span),

suggesting that the observed relationships with visual working memory capacity reflects more than general cognitive decline.

Value-driven attentional priority has been shown to be represented in the basal ganglia in healthy adults (Anderson, Laurent, & Yantis, 2014). Motor function was assessed in the present study because the basal ganglia are targeted by HIV once it enters the central nervous system, leading to decreased dopamine levels (Aylward et al., 1993; Becker et al., 2011; Berger et al., 1994; Dal Pan et al., 1992; Navia et al., 1986; Sardar et al., 1996). Interestingly, dopamine downregulation is also a prominent feature of substance dependence (e.g., Volkow, Fowler, & Wang, 2003), which is itself associated with increased sensitivity to value-driven attentional capture (Anderson et al., 2013). Such decreases in dopamine levels may lead to a reduction in reward sensitivity, which in turn more strongly motivates reward seeking and related attentional processes, perhaps reflecting a risk factor common to HIV+ and substance dependence. We found that slower finger tapping was associated with more pronounced attentional capture by irrelevant reward information.

Interestingly, value-driven attentional capture was not related to HAND stage or Karnofsky performance status. This suggests that difficulty ignoring previously reward-associated stimuli is not reducible to general neurocognitive decline in HIV. Instead, value-driven attentional bias reflects a sensitive indicator of HIV-risk that is related to the integrity of specific abilities that can decline with HAND.

Value-driven attentional capture was robust when assessed on the same day that reward learning occurred. Upon returning six months later, however, the effect of this reward learning was no longer evident at the group level, which contrasts with the persistence of value-driven attention evident in healthy young adults (Anderson & Yantis, 2013). Interestingly, and somewhat surprisingly, individual differences in the effect of the distractors on performance during this second assessment was still reliably predicted by several variables, including impulsiveness, history of substance dependence, performance on the finger tapping task, and prior awareness of the reward contingencies. This helps to explain the observations within the negative range of attentional capture at the 6-month follow-up assessment. In fact, performance was actually *better* (search was faster) in the presence of the previously reward-associated distractors during the second assessment for participants who were aware of the relationship between color and value, with a similar pattern existing for participants without a history of substance dependence. These findings, which were not predicted, suggest the intriguing possibility that certain participants were able to actively inhibit selection of the previously rewarded stimuli, perhaps as a part of an avoidance strategy. There is some evidence for inhibition of drug-associated stimuli in successful abstainers (e.g., Field & Cox, 2008; Stromark et al., 1997). As the participants in the present study were quite stable as a group, with very high treatment compliance and successful abstinence from illicit drugs as measured via urine drug testing and self-report, their stability may be related to an ability to actively suppress attentional capture by high-value stimuli that run counter to current goals. Consistent with such a suppression account of performance during the second visit, participants who were aware of the reward contingencies during training showed significantly improved target detection in the presence of high-value distractors. The fact that such suppression was only evident during the second

visit suggests that it depends either on practice ignoring particular reward stimuli (acquired during the first visit) or on the manner in which value associations are consolidated in long-term memory.

In a previous study, we demonstrated that value-driven attentional capture was more pronounced in individuals currently in treatment for drug dependence (Anderson et al., 2013). Here, we show more pronounced attentional capture in individuals with a history of substance dependence even though none of these individuals were actively using drugs. This is consistent with heightened susceptibility to value-driven attentional capture reflecting a trait-like characteristic that is not contingent upon active drug use and its acute effects on the brain.

There are several limitations that need to be considered when interpreting the results of the present study. First, the demonstrated correlations cannot be taken as evidence of causality. There is no direct evidence that attentional biases actually lead to impulsive behaviors or drug abuse. In this regard, however, it is interesting that prior (i.e., the 12 months leading up to diagnosis) rather than current non-planning impulsiveness significantly predicted capture. Similarly, strong value-driven attentional bias may reflect a phenotype that predisposes an individual to drug abuse and other risky and impulsive behaviors, a consequence of changes to the dopamine system resulting from drug abuse and/or HIV-related damage to the basal ganglia as described earlier, or both. Although more general measures of attentional control (Bellgrove & Mattingly, 2008) and the influence of reward on cognition (Cools, 2008) have been linked to genetic variability, the genetic underpinnings of susceptibility to value-driven attentional capture has not been directly investigated.

The present study focused on understanding individual differences among patients, without a control sample for comparison. This makes it difficult to know the degree to which the observed relationships are specific to HIV. We argue that value-driven attentional bias reflects a measure that is useful for understanding HIV risk and the neurocognitive consequences of HIV, but suspect that the findings reflect a broader tendency to engage in risky reward-motivated behaviors that is not uniquely linked to issues surrounding HIV.

Additional limitations include the use of a self-report measure to examine impulsiveness and the use of retrospective measures of risky behavior leading up to HIV+ diagnosis. For the retrospective measure of impulsiveness, participants may have inflated their ratings based on the assumption that their contraction of HIV was the result of impulsive behaviors. However, such inflation would not account for inter-individual differences in impulsiveness. Participants may have also biased their ratings based on more recent behavior, with the retrospective assessment strongly reflecting current impulsiveness. In this regard, it is noteworthy that only 42% of the variance was shared between current and prior non-planning impulsiveness, and that prior non-planning impulsiveness proved to be a more reliable predictor of attentional capture. It is difficult to know the degree to which participants' perceptions of how often they engage(d) in impulsive behaviors as measured by the BIS-11 translates to the specific behaviors that place one at risk for contracting HIV. Our measure of prior substance dependence is also only as valid as what participants both

accurately remembered and were willing to disclose to the experimenter; however, we chose to define substance dependence history broadly (presence vs absence) for this reason.

In light of these limitations, it would be informative for future research to investigate whether the degree to which reward-associated stimuli capture attention can predict future drug abuse, HIV-risk behaviors, and contraction of HIV. Similarly, future research might seek to track attentional biases as cognitive function declines with HAND. The study of more recently diagnosed HIV+ patients would also reduce the potential impact of memory bias, providing a more precise measure of impulsiveness surrounding contraction of HIV.

An intriguing possibility suggested by the present findings is that the ability to eventually inhibit the processing of high-value but currently task-irrelevant stimuli may reflect a trait related to the ability to exert control over impulsive behavior. The relationship between such inhibition and awareness of the reward contingencies suggests that it may be influenced by explicit strategy. The role of inhibitory processing in the management of behavior would therefore be another potentially fruitful direction for future research.

The findings of the present study contribute to our understanding of the cognitive processes that underlie high-risk reward-motivated behaviors associated with the contraction of HIV. We show that in HIV+ individuals, attentional bias for reward information was predicted by a patient's retrospective history of impulsive and risky behaviors in the months leading up to HIV+ diagnosis. Thus, increased susceptibility to value-driven attentional capture represents a potential risk factor for acquiring HIV. In addition, specific cognitive and motor abilities known to decline as a consequence of HIV infection were also related to value-based attentional biases, suggesting that the biobehavioral consequences of HIV might also influence how reward information is processed. Taken together, the present study provides strong evidence linking value-based attentional processing to HIV. A clearer understanding of this link and how the neurobiological consequences of HIV affect information processing may afford new insights into HIV risk and prevention.

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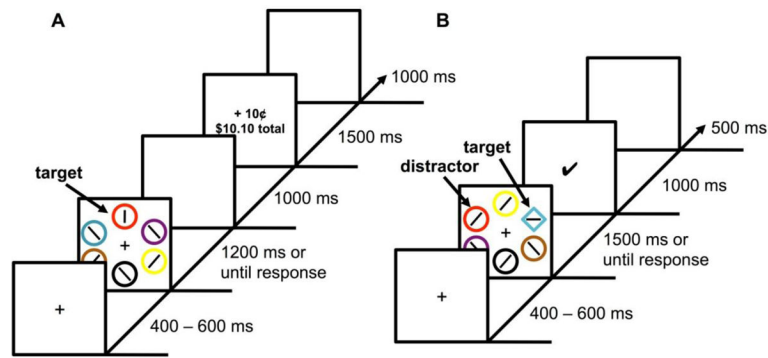
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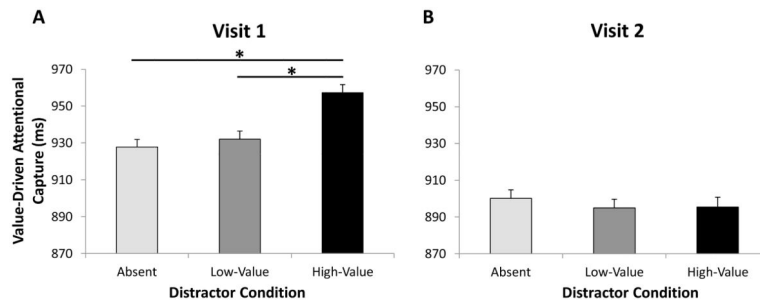


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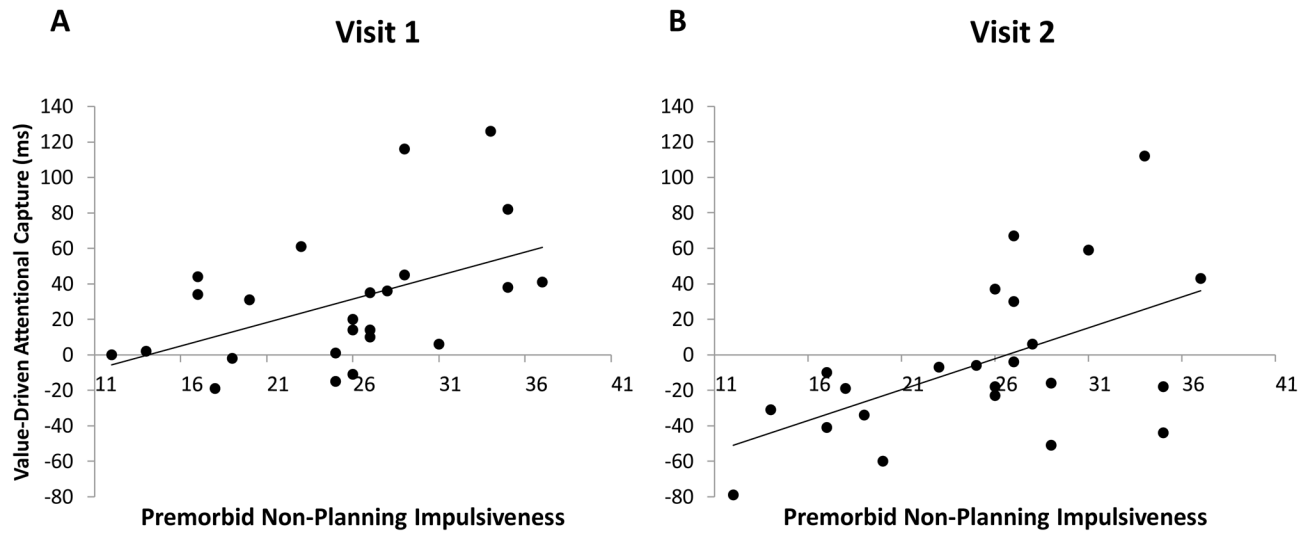


**Figure 1.**

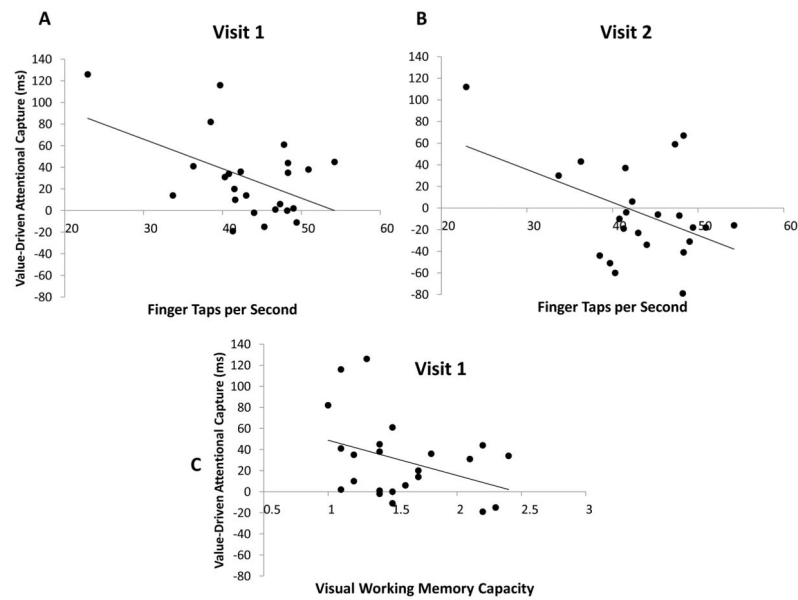
Sequence of events and time course for a trial during the training phase (A) and test phase (B) of the visual search task. During the training phase, participants searched for a target circle that was unpredictably red or green, and received a monetary reward for correctly reporting the orientation of a bar contained within the target. During the test phase, participants searched for a target defined as the unique shape (e.g., diamond among circles), and no monetary rewards were provided. On a subset of the trials, one of the non-target shapes was rendered in the color of a formerly reward-predictive target (i.e., red or green), which served as the reward-associated distractor.



**Figure 2.** Response time across the three distractor conditions in the test phase during Visit 1 (A), immediately following reward training, and Visit 2 (B), six months following reward training. Error bars reflect the within-subjects standard error of the mean. \* $p < 0.01$ .



**Figure 3.** Correlation between self-reported non-planning impulsiveness during the twelve months leading up to HIV+ diagnosis and value-driven attentional capture (slowing in RT caused by the presence of a high-value distractor) measured during Visit 1 (A), immediately following reward training, and Visit 2 (B), six months following reward training.



**Figure 4.** Relationship between attentional bias and measures of cognitive and motor functioning. Correlation between performance for the dominant hand on the finger tapping task and value-driven attentional capture (slowing in RT caused by the presence of a high-value distractor) measured during Visit 1 (A), immediately following reward training, and Visit 2 (B), six months following reward training. (C) Correlation between visual working memory capacity and value-driven attentional capture measured during Visit 1.

**Table 1**

Mean lifetime exposure to substances for the previously substance-dependent participants as determined from a structured clinical interview. Additional substances were reported, but amounts were considered negligible.

<b>Substance</b>	<b>Exposure</b>
<i>Lifetime Alcohol Exposure (l)</i>	3830.2
<i>Lifetime Nicotine Exposure (pack years)</i>	9.5
<i>Lifetime Marijuana Exposure (g)</i>	5087.5
<i>Lifetime Opioid Exposure (g)</i>	558.0
<i>Lifetime Cocaine Exposure (g)</i>	2048.7

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