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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.

1. Introduction

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, 2015a, 2015b). 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 and 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 et al., 2011a, 2011b; Hickey et al., 2010). Our ability to process sensory information is capacity-limited, and attention selects which among multiple competing sources of information receive representation (Desimone and Duncan, 1995). Once a stimulus has been learned to predict a reward, a persistent tendency to preferentially attend to that stimulus develops (Della Libera and Chelazzi, 2009; Peck et al., 2009; Raymond and 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, 2014a, 2014b; Anderson and Yantis, 2012). We refer to this consequence of

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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 and Cox, 2008; Lubman et al., 2000; Mogg et al., 2003; Stromark et al., 1997). Patients who show the largest attentional biases for drug-related stimuli are the most likely to relapse during the course of treatment (Carpenter et al., 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 et al., 2013). This effect was similar to the differential attentional processing attributed to drug cues (e.g., Carpenter et al., 2006; Field and 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 et al., 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, 2015a, 2015b).

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 et al., 2014a; Gottlieb et al., 2014; Yamamoto et al., 2013; see also Nickolaou et al., 2013), a region of the brain strongly affected by HIV and linked to associated motor control symptoms (Aylward et al., 1993; Berger et al., 1994; Dal Pan et al., 1992; Navia et al., 1986; Sardar et al., 1996). In addition, individuals with lower visual working memory capacities are especially prone to attentional capture (Fukuda and Vogel, 2009), including attentional capture by reward-associated stimuli (Anderson et al., 2011b, 2013; Anderson and 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 et al., 2002; Arendt et al., 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 et al., 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 toward previously reward-associated stimuli has been shown to persist for up to nine months without further training in healthy college-age individuals (Anderson and 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.

2. Material and methods

2.1. 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 and 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 et al., 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 et al., 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 min, hepatitis C status that required current medication, and use of prescription stimulants.

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