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The Role of HIV Infection, Cognition, and Depression in Risky Decision-Making

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Abstract

The authors examined the impact of HIV, cognitive dysfunction, and depression on decision-making. HIV+ (N=100) and HIV– (N=26) participants were administered a comprehensive neuropsychological battery, a modified version of the Iowa Gambling Task, and a measure of depressive symptoms. HIV+ participants demonstrated more difficulties in learning the gambling task than did HIV– participants. Executive functioning and depression emerged as strong predictors of gambling task performance. Depression partially mediated the relationship between executive functioning and gambling performance. Our findings suggest that HIV infection, executive dysfunction, and depression place individuals at risk for poor decision-making.

Decision-making involves collecting information about the expected valences, alternatives, and probabilities of available response options. Disruption to any of these component processes may result in risky behavior. The neurobiological circuitry underlying social decision-making includes such areas as the ventromedial prefrontal cortex (vmPFC) and insular cortex.¹ Patients with disruptions to the ventromedial cortex more frequently demonstrate impairments in social decision-making, in spite of otherwise largely-preserved intellectual abilities.^{2,3} Tasks that measure social decision-making (i.e., weighing of risk and benefits) have demonstrated both selectivity and sensitivity to ventromedial-prefrontal cortex lesions. Poor performance on decision-making can persist despite relatively unimpaired performance on tasks of planning and problem-solving that reflect dorsal-lateral prefrontal functioning (e.g., the Wisconsin Card-Sorting test), suggesting different neuroanatomical circuitry that subsumes these related, yet dissociable, processes. One such instrument, the Iowa Gambling Task (IGT), was developed in order to investigate the decision-making strategies in individuals with frontal lobe lesions. The task includes four decks of cards from which to choose, with each selected card resulting in either winning or losing a sum of “replica” money. Two out of the four decks will result in a net profit by the end of the task (i.e., Safe decks), whereas card selection from the other two will ultimately result in a loss (i.e., Risky decks). The decks that result in the net loss, however, offer larger payoffs early in the task than the others. Through its design, this task assesses participants’ capacity for decision-making and risk-taking by tracking which decks they draw from, thereby measuring their responses to reward/punishment and concern for future outcomes.

Decision-Making Among HIV+ Adults

The pattern of neuropsychological deficits typically observed in HIV+ individuals is consistent with frontal-striatal dysfunction (i.e., difficulties with attention and concentration,

information-processing speed, motor functioning, and executive functioning).⁴ There is also evidence that poor decision-making is prevalent among this population.^{5,6} Where HIV can result in problems with decision-making, individuals who contract HIV tend to engage in greater risk-taking practices in general, which makes this population ideal for studying decision-making performance.⁷ Hardy and colleagues⁵ administered a modified version of the IGT to a group of HIV+ patients and seronegative control subjects. HIV+ patients performed worse on the gambling task than controls. Similarly, among substance-dependent HIV+ individuals, deficits have also been observed in decision-making.^{6,8} Decision-making performance on the IGT moderated the relationship between emotional distress and reported sexual risk among HIV+ individuals, such that better performance on the IGT and greater distress predicted greater sexual risk-taking.⁹ However, among individuals with worse IGT performance, there was no significant relationship between distress and reported sexual risk, suggesting that emotional distress in isolation does not play a critical role in poor IGT performance. In other words, intact neural circuitry subserving decision-making is critical in order for emotional distress to have an influence on the functioning of this neural circuitry, thereby increasing risk-taking behavior. Overall, results support the contention that HIV+ individuals are at risk for poor decision-making behavior.

Depression, Cognition, and Decision-Making

Depression is considered to be one of the neuropsychiatric features associated with HIV.^{10,11} Although a number of studies have linked depression to impairments in executive functioning, attention, memory, and psychomotor speed,¹² such associations are not consistent, and many studies have failed to find direct associations between symptoms of depression and cognitive dysfunction.^{13–15} Inconsistencies across studies may be due to methodological differences in how depression is diagnosed, measured, reported, or handled, with regard to severity.¹⁶

Nevertheless, what is consistent, and of particular interest to the current study, are findings supporting dysfunction in decision-making in depressed patients.¹⁷ For instance, among depressed adolescents, Han and colleagues found impairments in both non-emotional areas of cognitive functioning (sustained attention and conflict-processing) as well as emotionally-laden domains (affective decision-making), with the latter being more associated with current mood state.¹⁸ Furthermore, deficits in emotionally-charged decision-making tasks have also been observed in chronic pain patients with depression. There is considerable evidence that depression leads to biases in processing emotional information that can result in poorer performance on an affective Go/No-Go task.^{19,20}

It is thought that depressed individuals are less likely to respond to negative feedback from the environment because of an decreased sensitivity to punishment,^{21–24} difficulties in recognizing rewards,²² or an inability to maintain reinforced behavior.^{25,26} This, in turn, can result in poor performance on decision-making or learning tasks, particularly when the outcome is unclear or misleading.²⁷ Depressed patients may have difficulty with flexible decisions-making requiring them to change their response choices when a previously disadvantageous choice becomes advantageous, and vice versa.^{17,28} Together, these studies suggest that depression may adversely affect social decision-making despite relatively intact cognition.

The extent to which cognition affects decision-making is only a small component of understanding the underlying processes involved in decision-making. Other variables linked to both cognition and decision-making may explain the process by which cognition actually influences decision-making. A variable may be termed a mediator “to the extent that it accounts for the relation[ship] between the predictor and the criterion.”²⁹ Although

cognition and depression have been linked to poor decision-making, it is unclear whether mild disturbances in cognition (such as those typically reported by HIV+ patients) affects poor decision-making, or other variables, such as depression, modulate the relationship between the two constructs.

The purpose of the current investigation was to examine decision-making performance among HIV+ and HIV– individuals and to determine which cognitive and psychiatric features, if any, are associated with decision-making. It was expected that HIV+ individuals would demonstrate more poor decision-making choices than HIV– individuals. It was also expected that gambling task performance would be correlated with executive dysfunction and depressed mood. Finally, we expected depression to partially mediate the relationship between cognition and decision-making (as assessed by gambling performance).

METHOD

Participants

Before data collection, all study procedures were approved by UCLA Institutional Review Board. Participants consisted of 126 HIV+ (N=100) and HIV– (N=26) individuals, who were recruited from various community clinics in the Los Angeles area. Exclusionary criteria included history of neurological disorder (e.g., head injury with loss of consciousness in excess of 60 minutes, stroke or seizure disorder, and CNS opportunistic infections). All participants were required to demonstrate at least a 6th-grade reading level and provide written informed consent. (See Table 1 for sample demographics.)

Neuropsychological Assessment

All participants were administered a comprehensive neuropsychological battery. Raw scores were converted to demographically-corrected T-scores (Table 2), which were then combined to create domain scores for the areas of attention and working memory, information-processing speed, learning and memory, motor, and executive function, by use of validated approaches.⁴

Gambling Task

The gambling task used in the present study is modeled from that of Bechara and colleagues.³⁰ Participants are told that 1) the goal of the task is to maximize profit on the loan of play money; and 2) they are free to switch decks whenever and as often as they desire. They are not told how many cards they are allowed to select (the game is over after 100 cards are selected). The ultimate yield is smaller for the higher-paying decks, A and B, because of larger penalties. The ultimate yield is larger for the lower-paying decks, C and D, because of the smaller penalties. Thus, participants must discriminate between short-term and long-term consequences. The Gambling Task has been used in a variety of populations, including the HIV population^{5,8} and has demonstrated convergent validity with attention and executive functions³¹ and ecological validity among drug-abusers.³² To examine whether participants were able to learn to discriminate between short-term and long-term consequences, a learning index was created by subtracting the average number of advantageous cards (i.e., decks A and B) selected from the first two blocks of 20 cards from the average of advantageous cards for the last three blocks. The learning-index approach is based on the idea that subjects' performance on the latter trials of the gambling task should reflect a more systematic approach to card-selection than earlier trials. Given this, it is expected that as participants adjust to the task (first two blocks of 20 cards), card selection occurs in a haphazard, less systematic fashion. Conversely, for subjects with intact decision-making ability, selection over the last three blocks will demonstrate a more systematic approach, which reflects learning. In other words, as the task progresses and participants are

exposed to rewards and losses, they will become better able to anticipate risky versus safe choices. Hence, it is expected that the last three blocks should show increases in the number of advantageous cards selected. The learning index represents the “net” amount of learning that takes place over the course of the task.

Depression

Depressive symptoms were measured with the Beck Depression Inventory–II (BDI–II).³³ The BDI–II is a 21-item, self-report rating scale that asks about the presence and prominence of cognitive, affective, and somatic symptoms of depression over the past week. Scores on each item can range from 0 (symptom absent) to 3 (presence of symptom is pronounced), yielding a possible range of BDI Total scores of 0 to 63. Total BDI–II score was used for statistical analyses. Given the overlap between somatic complaints reported as a function of HIV illness and somatic items on the BDI–II, we split BDI–II items into three factors: mood/motivation disturbance, self-reproach, and somatic disturbance, by use of procedures described by Castellon and colleagues.³⁴

Research Design and Statistics

This is a contrasted-groups study that used multiple regression and nonparametric statistics (Mann-Whitney *U*) to examine differences between HIV+ and HIV– participants on premorbid intellectual functioning (IQ), neuropsychological performance (NP), depression, and gambling performance. First, we examined the contributions of confounding variables to our study findings. Given that HIV+ and HIV– participants significantly differed on premorbid IQ ($U=668.50$; $p < 0.0001$), multiple regression was conducted to determine whether HIV status continued to predict the variation in neuropsychological performance, depression, and gambling performance beyond that of premorbid intellectual ability. There was also a disproportionately higher number of African Americans in our sample of HIV+ participants ($\chi^2[5]=21.47$; $N=126$; $p < 0.001$). Therefore, we examined ethnic differences between African Americans and other ethnic groups in neuropsychological test performance and IGT performance by use of analysis of variance (ANOVA). Next, two-tailed, bivariate Pearson correlations were used to examine relationships between NP, depression, and gambling performance for both status groups. Finally, multiple linear-regression analysis was conducted with our HIV+ patients to examine predictors of gambling performance. Before running multiple-regression analyses, all variables were inspected to ensure that statistical assumptions were met. For multiple regression, executive functioning was entered into the first step (as executive functioning demonstrated the strongest relationship to gambling performance), and depression in the second step. We examined the significance of R^2 change and corresponding β weights to determine whether depression mediated the relationship between cognition and gambling performance. In order to correct for multiple comparisons, the false-discovery rate (FDR) approach was used to correct for multiple comparisons made in primary study analyses.³⁵ Instead of controlling for the chance of any false positives (e.g., the Bonferroni method), FDR controls for the expected proportion of false-positives within a total number of comparisons.

RESULTS

HIV Status, Neuropsychiatric Performance, and Gambling Performance

There were no significant differences between drug-history groups (past use versus no use) on neuropsychological functioning and gambling performance. After controlling for premorbid IQ, HIV status did not significantly contribute to the variation in neuropsychological performance, ($\Delta r^2=0.004$; $p=0.201$). However, HIV status continued to predict the variance in gambling performance after controlling for premorbid IQ ($\Delta r^2=0.043$; $p=0.01$), suggesting that participants' HIV status contributes to performance on the

gambling task. Analysis of group differences revealed that HIV+ participants demonstrated more difficulty with learning on the gambling task than HIV- participants ($U=758.0$; $p=0.002$; Table 1 and Figure 1). As stated previously, given the disproportionate number of African Americans in the HIV+ group, we examined ethnic differences on neuropsychological performance and gambling performance. We found ethnic differences in global neuropsychological performance ($F[5,120]=5.233$; $p < 0.001$). Post-hoc analyses demonstrated that African Americans performed significantly worse than Caucasians (least significant difference [LSD] = -5.013 ; $p < 0.001$). However, there were no significant ethnic differences in IGT performance ($F[5,120]=1.33$; NS). Analysis of covariance (ANCOVA) revealed that ethnic differences in neuropsychological performance no longer remained significant after controlling for premorbid IQ ($F(5,119)=0.773$; NS).

For the entire sample, gambling learning index score was positively associated with attention and working memory ($r[125]=0.18$; $p=0.05$) and executive functioning ($r[125]=0.25$; $p < 0.001$).

HIV Status, Depression, and Gambling Performance

HIV+ patients endorsed more symptoms of depression than did HIV- patients ($F[1, 125]=14.70$; $p < 0.001$). HIV+ participants demonstrated significantly higher scores on mood/motivation disturbance ($U=4,629.0$; $p < 0.0001$), self-reproach ($U=3,801.0$; $p < 0.0001$), and somatic disturbances ($U=3,231.0$; $p < 0.0001$) than HIV- participants. Given that HIV+ participants demonstrated significantly higher scores on each dimension of the BDI-II, the total BDI-II score was used in subsequent analyses. Depression was negatively associated with gambling learning-index score ($r[125] = -0.27$; $p < 0.001$). Analysis of depression symptoms and gambling performance revealed that whereas both groups demonstrated similar effect sizes (HIV+: $r[100] = -0.23$; $p=0.02$); HIV-: $r[26] = -0.20$; NS), the relationship was only statistically significant for HIV+ patients. Evaluation of effect sizes for both groups indicates that depression affects gambling performance.

Predictors of Gambling Performance Among HIV+ Patients

Executive functioning held the strongest relationship with gambling performance ($r^2=0.062$; $p < 0.001$; $\beta=0.250$) and was also predictive of depressive symptoms ($\beta = -0.124$). Therefore, executive functioning was used in the partial mediation model, with depression and gambling performance. Depression predicted gambling performance after controlling for executive functioning ($r^2=0.110$; $p < 0.001$; $\beta = -0.226$). Inspection of standardized β weights associated with both direct and indirect effects of executive functioning on gambling performance revealed that depression partially mediated the relationship between executive functioning and gambling performance ($\beta=0.126$). Figure 2 depicts the mediation model.

DISCUSSION

This study compared the impact of depression and cognition on decision-making in a cohort of HIV+ and HIV- adults. Using a learning index, we examined how various factors, such as HIV status, cognition, and depression, interfered with participants' ability to learn on a decision-making task. Findings from this study extend the current literature by demonstrating the role of depression symptoms in decision-making and how emotional distress may result in problems in learning from rewards and punishments in spite of intact cognition. Consistent with findings in other studies,^{5,8,36} HIV+ individuals demonstrated poorer neuropsychological functioning, including decision-making (assessed by a modified version of the Iowa Gambling Task), as compared with seronegative individuals.

Decision-making was associated with attention and executive functioning for the entire sample, which is consistent with several previous studies,^{5,6} although not all.^{8,37} Further analysis into the relationship between discrete cognitive functions and gambling task performance demonstrated that executive functioning was most strongly associated with gambling performance, which is not particularly surprising, given that successful performance on the gambling task requires processes (i.e., flexible appraisals of the affective significance of stimuli, learning, and problem-solving) that are largely subserved by frontostriatal functions.

HIV+ individuals demonstrated higher levels of depression symptoms, which is consistent with other studies examining rates of depression among HIV+ and HIV- individuals.¹¹ Depression symptoms were strongly related to gambling-task performance, which is also consistent with Damasio's somatic marker hypothesis, which asserts that emotional processes (anticipatory affective signals/somatic states) can guide or bias decision-making,³⁸ and with previous studies that have demonstrated that depressed individuals have decreased response to negative feedback.²³ In addition to decreased sensitivity, allocation of cognitive resources becomes reduced, which results in deficits in remembering and engaging in other effortful cognitive processes.³⁹ Thus, deficits become more evident in effortful tasks, rather than tasks that involve automatic processes, which may partially explain inconsistent findings related to depression and cognition.

Successful performance on the gambling task requires the generation of autonomic responses, signaling emotional identification of choices made and the rewards and penalties received as a consequence of choices.³ Moreover, there is increasing evidence suggesting that depressed individuals appear biased in favor of high-risk/high-reward options.^{40,41} Depression, in itself, involves poor flexibility in shifting behavior when reward conditions change, which supports the hypothesis that depression could involve a rigid, generalized strategy for responding to reward, regardless of changes in contingencies, and with models emphasizing that decreases in positive affect are a fundamental characteristic of depression and lack of response to rewards.⁴²

It has been suggested that the gambling task measures different types of decisions. More specifically, there may be a differential influence of affective processes and executive functions, depending on whether decisions are made under ambiguity (e.g., first trials of the gambling task) or under risk (e.g., latter trials of task).^{43,44} In the current investigation, learning differences due to HIV status, cognitive impairment, or depression symptoms did not emerge until the latter trials of the task, which is when participants are expected to distinguish between risky versus safe decks. It is of particular interest that depression partially mediated the relationship between decision-making and executive functioning, demonstrating the importance of depression symptoms to decision-making processes. Our partial mediation model supports the contention that that emotional distress, even at a subclinical level, may be associated with risk-taking among those with intact executive functioning.⁹ Furthermore, our results demonstrate that affective disturbance has profound effects on decision-making. Engaging in risk-behaviors or decreases in sound judgment may be an early sign of depression. Practitioners working with HIV-infected individuals should be sensitive to declines in judgment because these can signal depression, which can be aggressively treated through pharmacotherapy, evidenced-based psychotherapy, or a combination of the two methods.

We recognize that the current study design is limited with regard to addressing the "chicken/egg" problem; that is, whether depression associated with HIV status causes decision-making impairments on the gambling task, or whether individuals with HIV evidence pre-morbid difficulties with decision-making, which placed them at risk for infection and

subsequent depressed mood. Our HIV+ participants were more likely to report past substance abuse, which suggests that this population may be more prone to engaging in risky behaviors in general. Furthermore, we were unable to target individuals with syndromic levels of depression (such as those diagnosed with Major Depressive Disorder), as most of our participants' BDI-II scores ranged from mild to moderate classifications of severity. Therefore, it is possible that relationships between executive dysfunction and depression may be, in part, influenced by mood severity. Moreover, alterations in reward choice and behavior may play a role in the continuity of depressive symptoms and, consequently, poor decision-making. Studies using a longitudinal investigation with a sample of individuals with clinically diagnosed major depression would be ideal to address this issue.

Although it could be argued that the observed relationships between cognition, depression, and decision-making are solely generalizable to the HIV+ population (because of the lack of significant findings in the HIV- population), we believe that the moderate effect sizes observed support their importance in decision-making for both subgroups. Although the relationships between these variables failed to reach statistical significance for the HIV- subgroup, this was largely due, in part, to small sample size (N=26). We recognize that a larger sample of controls would have been ideal, and that this is indeed a limitation to the current study. Nevertheless, despite this limitation, our findings are in accordance with the extant literature that has demonstrated that relationships between cognitive dysfunction and depressed mood affect performance on effortful cognitive tasks, and the findings extend previous work by demonstrating how dysphoric mood plays a partially mediating role in cognition and decision-making.

Taken together, our findings demonstrate the unique and shared affective and cognitive components involved in decision-making among a sample of HIV+ and HIV- individuals. This is particularly important for determining who is at risk for poor decision-making and, consequently, adverse outcomes. HIV+ individuals are more likely to report higher levels of depressed mood and to demonstrate cognitive problems, making this subgroup particularly vulnerable to showing poor decision-making. Given this, understanding which mechanisms are involved in decision-making can help to identify where breakdowns in the decision-making process may occur. Clinicians working with a high-risk population, such as the HIV + population, should be aware that despite intact cognitive functioning, dysphoric mood can interfere with the ability to make sound judgments.

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FIGURE 1. Performance on Gambling Task of HIV-Status Groups

Number of advantageous cards was computed by subtracting the number of risky cards selected from the number of safe cards.

FIGURE 2. Mediation Model (using standardized β coefficients)

The number of advantageous cards was computed by subtracting the number of risky cards selected from the number of safe cards.

TABLE 1

Sample Characteristics

Variable	HIV+ (N=100)	HIV- (N=26)
Age, years	43.83 (7.30)	46.31 (13.21)
Gender, % men	76.4	50
Ethnicity, % African American	68.8	43.1
Caucasian	17.3	44.8
Hispanic	9.1	8.6
Multiracial	0	1.7
American Indian	1.0	1.7
Asian American	1.4	0
Education	13.08 (2.3)	14.16 (2.13)
CD4 count	361.50 (248.32)	N/A
Undetectable viral load, %	33	N/A
* Premorbid IQ	103.01 (10.41)	111.30 (10.58)
*% Past substance use	61	31
Attention/working memory, T-score	42.56 (7.39)	48.05 (8.33)
Speed of information-processing	40.64 (9.52)	44.48 (9.69)
Learning and memory, T-score	38.02 (12.06)	44.83 (11.34)
Verbal function, T-score	45.57 (11.75)	46.95 (11.29)
Motor function, T-score	37.96 (10.85)	40.27 (10.48)
Executive function, T-score	41.51 (7.97)	46.24 (8.55)
Global functioning, T-score	41.08 (6.85)	45.11 (6.39)
* Depression score	14.53 (10.93)	8.36 (10.39)
* Gambling Index score	5.37 (18.84)	21.29 (23.80)

Values are mean (standard deviation), unless otherwise indicated.

* $p < 0.05$.

TABLE 2

Neuropsychological Battery and Normative Data

Cognitive Domain	Normative Data
Speed of information-processing	
Symbol Digit Modalities Test	Smith et al., 1982 ⁴⁵
Trail-Making Test Part A	Heaton et al., 1991 ⁴⁶
Learning and memory	
CVLT Trials 1–5	Delis et al., 1987 ⁴⁷
CVLT short-delay free recall	Delis et al., 1987 ⁴⁷
CVLT long-delay free recall	Delis et al., 1987 ⁴⁷
Verbal fluency	
Controlled Oral Word-Association Test	Heaton et al., 1991 ⁴⁶
Attention and working memory	
Paced Serial Addition Test	Stuss et al., 1988 ⁴⁸
Executive functioning	
Short Category Test, booklet format	Wetzel and Boll, 1987 ⁴⁹
Trail-Making Test Part B	Heaton et al., 1991 ⁴⁶
Stroop Color–Word Test–Interference	Heaton et al., 1991 ⁴⁶
Motor functioning	
Grooved Pegboard, dominant hand	Heaton et al., 1991 ⁴⁶
Grooved Pegboard, nondominant hand	Heaton et al., 1991 ⁴⁶

CVLT: California Verbal Learning Test.