Dopamine, depressive symptoms, and decision-making: the relationship between spontaneous eye blink rate and depressive symptoms predicts Iowa Gambling Task performance

Kaileigh A. Byrne¹ · Dominique D. Norris¹ · Darrell A. Worthy¹

Published online: 17 September 2015
© Psychonomic Society, Inc. 2015

Abstract Depressive symptomatology has been associated with alterations in decision-making, although conclusions have been mixed, with depressed individuals showing impairments in some contexts but advantages in others. The dopaminergic system may link depressive symptoms with decision-making performance. We assessed the role of striatal dopamine D₂ receptor density, using spontaneous eye blink rates, in moderating the relationship between depressive symptoms and decision-making performance in a large undergraduate sample that had not been screened for mental illness (N=104). The regression results revealed that eye blink rate moderated the relationship between depressive symptoms and advantageous decisions on the Iowa Gambling Task, in which individuals with more depressive symptomatology and high blink rates (higher striatal dopamine D₂ receptor density) performed better on the task. Our computational modeling results demonstrated that depressive symptoms alone were associated with enhanced loss-aversive behavior, whereas individuals with high blink rates and elevated depressive symptoms tended to persevere in selecting options that led to net gains (avoiding options with net losses). These findings suggest that variation in striatal dopamine D₂ receptor availability in individuals with depressive symptoms may contribute to differences in decision-making behavior.

Keywords Decision-making · Computational modeling · Dopamine · Depression · Iowa Gambling Task

Decision-making is prevalent in nearly every aspect of daily functioning, from major decisions such as career choices and financial planning to routine decisions such as whether to exercise or attend a social engagement. Despite the importance and frequency of decision-making, this process can be influenced by many factors, including mental disorders and affective states. One mental disorder that has been shown to impact decision-making is major depression (Paulus & Yu, 2012). The National Institute of Mental Health reported that in 2012 an estimated 16 million Americans exhibited at least one depressive episode in the course of the year, a rate that has more than doubled since the 1990s (Compton, Conway, Stinson, & Grant, 2006). Given the pervasiveness of depression and the importance of decision-making, in the present study we assessed the relationship between depression and decision-making and the possible role of striatal dopamine in moderating this relationship.

Theories aimed at identifying the neural and behavioral mechanisms of depression suggest that aberrations in reward and punishment responsiveness may contribute to depressive phenotypes (Beck, 1979; Elliott, Sahakian, Herrod, Robbins, & Paykel, 1997; Henriques & Davidson, 2000; Pizzagalli et al., 2009). Specifically, depression can be characterized by decreased sensitivity to reward feedback and altered sensitivity to punishment (Eshel & Roiser, 2010). Previous work has demonstrated that depressed individuals exhibit heightened attention to negative information and enhanced sensitivity to punishment feedback and losses (Berenbaum & Oltmanns, 1992; Carver, Johnson, & Joormann, 2008; Gotlib & Joormann, 2010; Mathews & MacLeod, 2005; Pizzagalli, Iosifescu, Hallett, Ratner, & Fava, 2008; Taylor Tavares et al., 2008), as well as decreased behavioral sensitivity to reward and ventral striatum activation in response to reward (Henriques, Glowacki, & Davidson, 1994; Eshel & Roiser, 2010; Pizzagalli et al., 2009; Robinson, Cools, Carlisi,
Sahakian, & Drevets, 2012). Given the extensive work on this theory, strong evidence suggests that altered reinforcement processing in depressed individuals may be due to differences in functioning of the striatum, a region involved in reward processing (Delgado, Nystrom, Fissell, Noll, & Fiez, 2000; Eshel & Roiser, 2010). Moreover, neuroimaging research has demonstrated that the striatum is able to distinguish between gain and loss feedback (Delgado et al., 2000). Because depression is characterized by altered reward and punishment responses, and striatal dopamine has been shown to underlie reward processing, it is reasonable to predict that striatal dopamine may influence decision-making in individuals with depressive symptoms (Delgado, 2007; Delgado et al., 2000). To investigate this hypothesis, we utilized the Iowa Gambling Task (IGT), a decision-making task that assesses risk preferences, responsibility to uncertainty, and gain and loss sensitivity. Both information processing and reward sensitivity are key components of decision-making, and therefore, the cognitive biases associated with depression directly impact decision-making processes. Although depressed individuals have shown deficits in some decision-making situations, including gain maximization tasks, they excel on tasks that rely on loss sensitivity, such as loss minimization tasks (Beevers et al., 2013; Cooper et al., 2014; Maddox, Gorlick, Worthy, & Beevers, 2012). Computational modeling results have indicated that depressed individuals are more likely to choose options with the smallest expected rewards under loss minimization conditions (Beevers et al., 2013). Thus, previous research on depression and decision-making has shown that individuals with elevated depressive symptoms have clear cognitive biases that lead to success in some decision-making situations, but failure in others.

Several studies have examined the relationship between depressive symptoms and the IGT. For example, previous work using the Hamilton Rating Scale for Depression to examine differences between clinically depressed individuals and healthy controls showed that depressed individuals selected the advantageous decks more than controls, earned more points on the task, and learned to avoid the high-risk decks faster (Smoski et al., 2008). Therefore, evidence suggests that depressive symptoms may actually confer an advantage in some decision-making contexts. However, other research has shown that individuals diagnosed with major depressive disorder (MDD) using the DSM-IV criteria perform worse on the IGT than do healthy controls (Cella, Dymond, & Cooper, 2010; Must et al., 2006). Specifically, depressed individuals selected more cards from the low-magnitude, high-frequency-of-losses disadvantageous Deck A, whereas control participants selected the high-magnitude, low-frequency-of-losses advantageous Deck D (Cella et al., 2010). Further work has supported this effect in adolescents, in that adolescents with MDD selected the advantageous decks less than did control group adolescents (Han et al., 2012). Although the research on depression and IGT performance has been mixed, with some studies showing that depressed individuals perform worse and others showing that they perform better on the task, the present study differs in three key ways. First, we used a sample of healthy volunteers and a different measure of depressive symptomatology. Second, we used a continuous measure of depression, rather than dividing the sample into groups, to better represent the range of depressive symptomatology in our sample. Finally, we measured spontaneous eye blink rates (EBRs) to indirectly assess striatal dopamine D2 receptor density as a potential moderator of depressive symptoms and decision-making performance on the IGT.

A key association between depression and decision-making can be attributed to the dopaminergic system. Dopamine regulates feedback processing and reward learning during decision-making (e.g., Brand, Labudda, & Markowitsch, 2006; Doya, 2008; Rolls, 2000; Schultz, 2006). Furthermore, dopaminergic striatal neurons have been shown to have a specific role in encoding reward prediction errors (Doya, 2008; Schultz, Dayan, & Montague, 1997). In a pharmacological research study of the relationship between dopamine and IGT performance, a branched-chain amino acid mixture was administered that resulted in decreased neural tyrosine availability and dopamine synthesis. The reduction in dopaminergic activity led to increased focus on immediate rewards and, consequently, poorer decision-making performance (Sevy et al., 2006). Similarly, a recent positron emission tomography (PET) study examining the relationship between amphetamine-induced ventral striatal dopamine release and decision-making performance showed a correlation between the magnitude of striatal dopamine release and advantageous selections on the IGT (Oswald et al., 2015). However, given the nature of the IGT, it could not be determined whether the decision-making deficits associated with elevated dopamine release (lower D2/D1 receptor binding potentials) should be attributed to increased reward sensitivity or reduced sensitivity to losses. In contrast to these studies showing that greater dopamine release was associated with suboptimal decision-making, additional work using PET imaging demonstrated that increased dopamine release in the ventral striatum predicted selection of the advantageous decks on the IGT (Linnet, Møller, Peterson, Gjedde, & Doudet, 2011). One potential difference in these findings, as Oswald and colleagues mentioned, was in the mechanisms underlying advantageous and disadvantageous performance on the IGT. Both hypersensitivity to reward and diminished loss sensitivity can result in suboptimal IGT performance, but examination of IGT performance differences alone makes it difficult to determine which reward-processing mechanism accounts for the performance effects. We therefore applied computational models to the data in the present work to assess specific strategies that underlie decision-making performance. In addition to work linking the dopaminergic system to the IGT, a large
body of research has demonstrated that dopamine moderates depressive symptoms (see Brown & Gershon, 1993; Depue & Iacono, 1989; Dunlop & Nemeroff, 2007; Kapur & Mann, 1992; and Rampello, Nicoletti, & Nicoletti, 2000, for reviews). Consequently, it is important to consider the interplay between both observed depressive symptoms and dopamine in predicting decision-making behavior.

In order to assess how dopamine may modulate decision-making behavior in depressed individuals, we utilized the spontaneous EBR. Although previous research had proposed that EBR is an indicator of striatal dopamine levels (Karson, 1983; Taylor et al., 1999), extensive pharmacological and behavioral work in both monkeys and humans has implicated the role of EBR as an indicator specifically of dopamine D1 and D2 receptor availability in the striatum (Elsworth et al., 1991; Groman et al., 2014; Jutkiewicz & Bergman, 2004; Kaminer, Powers, Horn, Hui, & Evinger, 2011; Kleven & Koek, 1996; Slagter, Georgopoulos, & Frank, 2015).

Although there has been evidence for the contributions of both D1 and D2 receptors, a recent pharmacological PET study compared the effects of D1 and D2 receptor agonists on the spontaneous EBR in male vervet monkeys (Groman et al., 2014). Their findings indicated that the spontaneous EBR was correlated with dopamine D2 receptor density in the ventral striatum and caudate nucleus, but no association with D1 receptors in the striatum was observed. They also found that D2 receptor density predicted learning from positive feedback during reversal learning. Behavioral evidence with humans supports the role of EBR as an indicator of D2 receptor availability (Slagter et al., 2015). However, in this study, which focused on the effect of spontaneous EBR on a probabilistic reinforcement-learning task, EBR predicted learning from negative outcomes. The authors reconciled their findings with those of the Groman group by suggesting that positive feedback sensitivity can result from negative prediction errors (Piray, 2011; Slagter et al., 2015).

Importantly, the findings from studies that have examined the relationship between EBR and depression have been inconsistent. Although some work has demonstrated that individuals with MDD and subvocal rumination have increased EBRs (Cruz, Garcia, Pinto, & Cechetti, 2011; De Jong & Merckelbach, 1990; Mackintosh, Kumar, & Kitamura, 1983), other studies have shown a different pattern of results. For example, in a study that compared 12 male individuals with MDD to 12 male healthy control participants, no differences between the groups were observed under normal conditions. Following sleep deprivation, however, the depressed individuals had higher EBRs than did the controls (Ebert et al., 1996). Additional work comparing two in-patient groups with MDD receiving either electroconvulsive therapy or antidepressant drugs showed that EBRs were elevated following treatment (Berrios & Canagasabey, 1990). A critical distinction between these previous studies on EBR and depression and the present investigation is that we utilized a large representative sample of males and females and examined a broad range of depressive symptoms. Because the previous studies have shown inconsistent results, we could not provide a clear hypothesis about the relationship between EBR and depressive symptoms; however, the results of this study will provide directional support for this relationship and clarify the inconsistencies in previous studies.

Therefore, in the present study, we sought to determine whether the spontaneous EBR modulates the relationship between depression and decision-making behavior. Although the research on depression and IGT performance has had mixed results, on the basis of prior work demonstrating that striatal dopamine D2 receptor density specifically regulates learning from negative outcomes, we predicted that increased D2 receptor density, as indexed by higher EBR, could result in decision-making benefits in individuals expressing depressed symptoms. This could account for the differences in decision-making performance noted in previous studies (Cella et al., 2010; Must et al., 2006; Smoski et al., 2008), whereby depressed individuals with lower D2 receptor density might perform worse on the IGT, and those with higher D2 receptor density might show enhanced IGT performance. In addition to examining the behavioral results of the IGT, we also applied reinforcement-learning models to the data in order to more critically determine the precise cognitive mechanisms underlying individuals’ decision-making behavior. Because altered reinforcement processing is a defining characteristic of depression, it is important to utilize these models in order to allow inferences about which aspect of reinforcement processing drives decision-making performance effects. From the computational modeling results, we could directly assess the degrees to which depression and D2 receptor density are linked to enhanced loss aversion and reward sensitivity in the task.

Method

Participants

The study was approved by the Institutional Review Board at Texas A&M University (approval number IRB2012-0719D) before any procedures were implemented. A total of 104 undergraduate students (54 females, 50 males; $M_{\text{age}}=18.81$, $SD_{\text{age}}=0.95$) were recruited from an introductory psychology course at Texas A&M University. To determine the sample size, we conducted a power analysis using G*Power 3.1.9.2 (Faul, Erdfelder, Buchner, & Lang, 2009) to determine the minimum sample size that would be needed to detect a medium-sized effect using a two-tailed alpha level of .05. Our main analysis of interest was a multiple regression with four predictors: our metric for symptoms of depression,
spontaneous eye blink, the interaction term between depression symptoms and spontaneous eye blink, and gender, which was included as a covariate. Power calculations indicated that our study design would require a sample size of at least 84 participants to achieve 80% power. With 95 participants, we would have 85% power. On the basis of this calculation, our goal was to collect a sample size of at least 100 participants, to account for data collection errors, smaller effect sizes than the one used in our power analysis, or other issues. We ran participants until we reached that number and then continued through the end of the work week. Students received partial course credit for completing the study.

Materials and Procedure

**Spontaneous EBR (dopamine D2 receptor marker)** In line with previous work (e.g., Chermahini & Hommel, 2010; Colzato, Slagter, van den Wildenberg, & Hommel, 2009; De Jong & Merckelbach, 1990; Ladas, Frantzidis, Bamidis, & Vivas, 2014), we recorded spontaneous eye blink using an electrooculogram (EOG). Following Fairclough and Venables (2006), vertical eye blink activity was collected by attaching Ag–AgCl electrodes above and below the left eye, with a ground electrode placed at the center of the forehead. All EOG signals were filtered at 0.01–10 Hz and amplified by a Biopac EOG100C differential corneal–retinal potential amplifier. In line with previous research, eye blinks were defined as increases in EOG amplitude greater than 100 μV and less than 500 ms in duration (Barbato et al., 2000; Colzato, Slagter, Spapé, & Hommel, 2008; Colzato et al., 2009a, b; Colzato, van Wouwe, & Hommel, 2007). Eye blink frequency was both manually counted and derived using BioPac Acqknowledge software functions, which computes the frequency of amplitude changes of greater than 100 μV, but not duration differences, in order to ensure valid results. The manual and automated EBRs were strongly positively correlated, r = .92, p < .001. Because the automated results were not sensitive to differences in duration and included only blinks less than 500 ms in duration, the manual EBR was used for all other statistical analyses.

All recordings were measured during daytime hours before 4 pm, because previous work had shown that diurnal fluctuations in spontaneous EBR can occur in the evening hours (Barbato et al., 2000). A black “X” was marked at eye level 1 m from where the participant was seated. Instructions were given for the participant to look in the direction of the marker for the duration of the recording and to try to avoid moving or turning the head. Eye blinks were recorded for 6 min under resting conditions. Each participant’s EBR was determined by computing the average number of blinks across the 6-min time interval. The individual EBRs ranged from 4.33–41.17 blinks/min (M=17.80, SD=8.34) in our sample, suggesting a wide range of dopaminergic functioning; this was similar to the range reported in previous work (Colzato, van den Wildenberg, van Wouwe, Pannebakker, & Hommel, 2009). A faster EBR is indicative of higher striatal dopamine D2 receptor density, whereas a slower EBR signifies lower striatal dopamine D2 receptor density.

**Depression Questionnaire** The 20-item Center for Epidemiological Studies–Depression Scale (CES-D) was employed to measure depressive symptomatology in our sample (Radloff, 1977). The CES-D is a reliable measure of depression with high internal consistency (α=.85). The overall reliability of the CES-D in our sample was similar to the norm (α=.90). Although not designed as a clinical diagnostic tool, a standard cutoff score of 16 on the CES-D scale, out of a maximum score of 60, is typically used to designate clinical from nonclinical levels of depressive symptoms. In the present study, the mean CES-D scale score was 17.31 (SD=9.54, range=2–49), suggesting that our sample contained a broad range of depressive symptomatology. It is important to note that these scores were reported at a single time point, and thus, the CES-D scores are not necessarily indicative of a clinical condition, but rather reflect depressive symptoms occurring in the past 7 days only.

Participants were given the standard CES-D scale instructions indicating that they would be shown a list of ways they might have felt or behaved. They were asked to respond how often they had felt those ways in the last 7 days. Participants responded on a scale from 0 (Less than 1 day) to 3 (5–7 days), and the questions included items such as “I felt that everything I did was an effort” and “I had crying spells.”

**Iowa Gambling Task** The decision-making instructions and task design were the same as those used in the original IGT version (Bechara, Damasio, Damasio, & Anderson, 1994). The IGT has been utilized to identify neurocognitive differences in individuals with lesions to the ventromedial cortex and amygdala (Bechara & Damasio, 2005; Bechara et al., 1994). Recent neuroimaging work has demonstrated that in addition to these neural regions, both the dorsal and ventral striatum—areas involved in reward processing—are activated during the IGT, indicating that the IGT is sensitive to differences in striatal function (X. Li, Lu, D’Argembeau, Ng, & Bechara, 2010).

The task instructions specified that the purpose of the task was to gauge how people use information to make decisions. Participants were asked to repeatedly select from one of four decks of cards, and that they could either gain or lose points on each draw. Each deck corresponded to a key on the keyboard. Participants began the task with 2,000 hypothetical dollars and were given a goal of earning at least $2,500 by the end of the task. They were not informed that the task included 100 trials of selections from one of the four decks of cards. Deck A offered a high magnitude of reward and a high frequency of...
losses (five loss trials equivalent to $250 each), with a net loss of $250 over every ten trials. Deck B yielded the same net loss as Deck A for every ten trials, but offered high-magnitude, low-frequency losses (one loss trial valued at $1,250), with a net loss over every ten trials of $250 dollars. In contrast, Decks C and D both offered a net gain of $250 across every ten trials. Like Deck A, Deck C gave frequent losses of low magnitude, but yielded more gains than losses overall. Similarly, Deck D provided infrequent losses of high magnitude, but offered more gains than losses over every ten trials. Thus, Decks A (high-magnitude reward, frequent losses) and B (high-magnitude reward, infrequent losses) were the disadvantageous decks, because they resulted in overall net losses, whereas Decks C (low-magnitude reward, frequent losses) and D (low-magnitude reward, infrequent losses) were the advantageous decks, because they yielded overall net gains. Table 1 shows the exact payoff structure for each deck across every ten trials. IGT performance was determined by computing the difference in proportions of advantageous versus disadvantageous deck selections [(C+D)−(A+B)] across all trials during the task. Although analysis of IGT performance is useful in assessing advantageous decision-making, it still remains unclear whether good performance on the IGT should be attributed to increased loss aversion, diminished sensitivity to reward, or perseveration in choosing net gains. In order to determine which reinforcement-processing strategies drive IGT performance effects, we applied computational models to our data.

Model descriptions Several models were fit to the data, including two single-term reinforcement-learning (RL) prospect valence learning (PVL) models, as well as a two-term RL valence-plus-perseveration (VPP) model. The VPP model has recently been shown to provide a significantly better fit to IGT data than do single-term models such as the PVL model, because it accounts for participants’ tendencies to both select options with relatively greater expected value and to persevere with options that have recently provided net gains (Ahn et al., 2014; Worthy, Pang, & Byrne, 2013). The PVL model (Ahn, Busemeyer, Wagenmakers, & Stout, 2008; Ahn, Krawitz, Kim, Busemeyer, & Brown, 2011) assumes that the weights given to gains and losses follow the assumptions of prospect theory (Kahneman & Tversky, 1979). The VPP model is similar to the PVL models, except that the terms for perseveration and expectancies are isolated as separate terms. A win–stay/lose–shift (WSLS) model was also included, to determine whether choices were determined strictly by the outcome of the previous trial (Worthy, Hawthorne, & Otto, 2013). The WSLS model assumes that an individual will persevere in selecting the same option if the previous trial resulted in a net gain, or will switch to a different option if the previous trial resulted in a net loss. Finally, a baseline, or random-responding, model was applied to the data, which assumes stochastic responses.

Prospect valence learning models We applied two PVL models to the data. Both models have four free parameters and include a utility function and a trial-independent action selection rule. However, in the first model, the PVL delta model, a value-updating rule was incorporated as a parameter in the model to update expected values on each trial. In the second model, the PVL decay model, rather than a value-updating parameter, a decay rule was included in the model, which assumes that the values of all options decay over time.

The prospect valence utility function assumes that the evaluation of each outcome on each trial operates in accordance with the utility function derived from prospect theory (Ahn et al., 2008; Kahneman & Tversky, 1979). The utility function exhibits decreasing sensitivity to increases in magnitude, as well as different sensitivities to losses versus gains. The utility on trial t, \( u(t) \), of each net outcome, \( x(t) \), was

\[
u(t) = \begin{cases} 
x(t)^\alpha & \text{if } x(t) \geq 0 \\
-\lambda |x(t)|^\alpha & \text{if } x(t) < 0 
\end{cases}
\]

(1)

Here, the utility function shape is determined by \( \alpha \), the shape parameter (\( 0 < \alpha < 1 \)), and \( \lambda \) represents the loss aversion parameter (\( 0 < \lambda < 5 \)) that governs loss sensitivity relative to gain sensitivity. A value of \( \lambda \) greater than 1 indicates that an individual is more sensitive to losses than to gains. Similarly, a \( \lambda \) value less than 1 signifies enhanced sensitivity to gains as compared to losses.

### Table 1 Reward schedule for the Iowa Gambling Task

<table>
<thead>
<tr>
<th>Draw from Deck</th>
<th>Deck A</th>
<th>Deck B</th>
<th>Deck C</th>
<th>Deck D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100</td>
<td>100</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>2</td>
<td>100</td>
<td>100</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>100, −150</td>
<td>100</td>
<td>50, −50</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td>100</td>
<td>100</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>100, −300</td>
<td>100</td>
<td>50, −50</td>
<td>50</td>
</tr>
<tr>
<td>6</td>
<td>100</td>
<td>100</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>7</td>
<td>100, −200</td>
<td>100</td>
<td>50, −50</td>
<td>50</td>
</tr>
<tr>
<td>8</td>
<td>100</td>
<td>100</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>9</td>
<td>100, −250</td>
<td>100, −1250</td>
<td>50, −50</td>
<td>50</td>
</tr>
<tr>
<td>10</td>
<td>100, −350</td>
<td>100</td>
<td>50, −50</td>
<td>50, −250</td>
</tr>
</tbody>
</table>

Cumulative payoff

See Bechara et al. (1994) for the full table of payoffs for the first 40 cards drawn from each deck. In the present task, the sequence was repeated for cards 41–80 and 81–100, so that a participant could potentially select the same deck on all 100 draws.
The action selection rule controlled the predicted probability that deck \( i \) would be chosen on trial \( t \), and was calculated using a Softmax rule (Sutton & Barto, 1998):

\[
Pr(i(t)) = \frac{e^{\theta(t)E_i(t)}}{\sum_{j=1}^{4} e^{\theta(t)E_j(t)}}.
\] (2)

The trial-independent action selection\(^1\) rule governed expected values and was represented as

\[
\theta(t) = 3^c - 1,
\] (3)

where \( c \) (0 ≤ \( c \) ≤ 5) is the response consistency or exploitation parameter. Larger values of \( c \) indicate that an individual has a greater tendency to choose options with higher expected values. Similarly, smaller \( c \) values indicate a greater tendency to explore options with lower expected values.

The PVL delta model included the value-updating rule, which determines how the utility \( u(t) \) is used to update expected values or expectancies \( E_i(t) \) for the selected option, \( i \), on trial \( t \). The delta rule assumes that expected values are recency-weighted averages of the rewards received for each option:

\[
E_i(t) = E_i(t-1) + \phi [u(t) - E_i(t-1)].
\] (4)

The recency, or learning rate, parameter \( \phi \) (0 ≤ \( \phi \) ≤ 1) defines the weight given to recent outcomes in updating expected values. Higher values of \( \phi \) denote a greater weight to recent outcomes.

Instead of the value-updating rule, the PVL decay model used the decay rule (Erev & Roth, 1998) in which expectancies of all decks decay, or are discounted, over time. The expected value of the selected deck is then added to the current outcome utility:

\[
E_i(t) = A \cdot E_i(t-1) + \delta_i(t) \cdot u(t).
\] (5)

The decay parameter \( A \) (0 ≤ \( A \) ≤ 1) determines the extent to which the previous expected value is discounted. \( \delta_i(t) \) is a dummy variable that is 1 if deck \( j \) is chosen and 0 otherwise. Thus, the utility shape (\( \alpha \)), loss aversion (\( \lambda \)), and exploitation (\( c \)) free parameters are common to both the PVL delta and decay models, whereas the recency free parameter \( \phi \) defines the PVL delta model, and the decay \( A \) free parameter defines the PVL decay model.

Valence-plus-perseveration RL model We used the PVL utility function (Eq. 1) and the delta rule from the PVL delta model (Eq. 4) to determine the expected reward value \( E_j(t) \) for each choice \( j \) for the two-term VPP model (Worthy et al. 2013). The VPP model includes seven free parameters: utility shape (\( \alpha \)), loss aversion (\( \lambda \)), exploitation (\( c \)), decay (\( k \)), recency or learning rate (\( \phi \)), gain increment (\( \epsilon_{\text{pos}} \)), and loss increment (\( \epsilon_{\text{neg}} \)) parameters. The perseveration \( P_j(t) \) strengths for each option \( j \) were determined by a more general form of the decay rule that had previously been used to model perseveration or autocorrelation among choices (Kovach et al., 2012; Schönberg, Daw, Joel, & O’Doherty, 2007). The perseveration term for chosen option \( i \) on trial \( t \) differed depending on whether the net outcome, \( x(t) \), was a positive or negative value:

\[
P_i(t) = \begin{cases} 
    k \cdot P_i(t-1) + \epsilon_{\text{pos}} & \text{if } x(t) \geq 0 \\
    k \cdot P_i(t-1) + \epsilon_{\text{neg}} & \text{if } x(t) < 0.
\end{cases}
\] (6)

Here the decay parameter \( k \) (0 ≤ \( k \) ≤ 1) is similar to the decay parameter \( A \) in Eq. 5 above for the PVL decay model. The tendency to perseverate or switch is incremented, each time an option is chosen, by \( \epsilon_{\text{pos}} \) and \( \epsilon_{\text{neg}} \) which were allowed to vary between −1 and 1. A tendency to persevere by choosing the same option on succeeding trials is represented by positive values, whereas negative values denote a tendency to switch. The values \( V_j(t) \) for each option \( j \) were the sums of the expected value and perseverative value from Eqs. 4 and 6. The combined values were entered into a Softmax rule to determine the probability of selecting each option, \( i \), on each trial \( t \):

\[
Pr(i(t)) = \frac{e^{\theta(t) V_i(t)}}{\sum_{j=1}^{4} e^{\theta(t) V_j(t)}}.
\] (7)

where \( \theta(t) \) is a free parameter that accounts for participants’ tendencies to exploit the highest-valued option or to select options randomly.

Win–stay/lose–shift model In addition to fitting the RL models described above, we also fit a WSLS model and a baseline model. The WSLS model has two free parameters and is identical to the model used in prior work from our lab (Worthy, Hawthorne, & Otto, 2013). The first parameter represents the probability of perseverating with the same option, \( i \), on the next trial if the net gain received on the current trial is greater than or equal to zero:

\[
P(i(t)|\text{choice}_{r-1} = i \& r(t-1) \geq 0) = P(\text{stay}|\text{win}).
\] (8)

Here \( r \) represents the net payoff received on a given trial, in which any loss is subtracted from the gain received. The probability of switching to another option following a win trial is \[ 1 - P(\text{stay}|\text{win}). \] To determine a probability of selecting each of
the other three options, we divided this probability by 3, so that the probabilities for selecting the four options summed to 1.

The second parameter represents the probability of shifting to another option $j$ on the next trial if the reward received from selecting option $i$ on the current trial is less than zero:

$$P(j, (t)|choice_{t-1} = i & r(t-1) < 0) = P(shift|loss).$$

This probability is divided by 3 and assigned to each of the other three options. The probability of staying with an option following a “loss” is $1 - P(shift|loss)$.

**Baseline model** Finally, the baseline model assumes fixed choice probabilities (Gureckis & Love, 2009; Worthy & Maddox, 2012). The baseline model has three free parameters that represent the probabilities of selecting Decks A, B, and C (the probability of selecting Deck D is 1 minus the sum of the three other probabilities).

**Procedure**

After providing written informed consent, participants began the experiment with 6 min of EBR recordings. After the EBR physiological measure, participants completed the CES-D depression questionnaire and the IGT decision-making task on PC computers using Psychophysics Toolbox for MATLAB (version 2.5; Brainard, 1997). Upon completion of the experiment, participants were debriefed about the nature of the study.

**Results**

**Statistical analyses**

Because previous research had shown gender differences in EBR (Dreisbach et al., 2005; C. S. R. Li, Huang, Constable, & Sinha, 2006; Müller et al., 2007; Mulvihill, Skilling, & Vogel-Sprott, 1997), we examined gender differences in our sample. Using an independent-samples $t$ test, we observed a significant gender difference in EBR in which females ($M=19.53$, $SD=9.05$) had a faster EBR than males ($M=15.91$, $SD=7.10$), $t(103)=2.27$, $p=.03$. Given the significant gender differences in EBR in our sample and those reported in prior studies, we included gender as a covariate in our regression analyses.

To determine whether learning occurred over the course of the IGT, we conducted a repeated measures analysis of variance with the average IGT performance for each of the five 20-trial blocks entered in the analysis. The results indicated a significant effect of learning across the task, $F(4, 4.16)=7.76$, $p<.001$ (Fig. 1). To evaluate whether our sample performed similarly to participants from previously published work, we compared our data with those of the control participants from Bechara et al.’s (2001) study, and from a sample of 504 participants across several published studies compiled by Steingroever and colleagues (2014). In comparison to the healthy control participants in previous research ($N=40$) with the IGT, in which 32.5% of participants had net scores of greater than $−.10$ (ten more disadvantageous than advantageous selections; Bechara et al., 2001), only 3.85% of our sample scored below $−.10$. Thus, our sample, including all individuals across the depressive symptoms spectrum, performed better on the IGT than the control sample in previous research. However, as compared to a large ($N=504$) sample of healthy participants from a recently published data pool, our sample ($M=−.01$, $SD=.26$) selected more disadvantageous options than the sample from the data pool ($M=−.08$, $SD=.32$), $t(608)=−2.62$, $p=.01$ (Steingroever et al., 2014). Given these two comparisons, the IGT performance from our sample appears to fall in between these two normative populations. In order to verify that our sample comprised a broad range of depressive symptoms, we determined that 52.89% (range=2–49) of the participants in our sample had CES-D scores of 16 or greater, indicating depressive symptoms in the clinical range. Figure 2 illustrates the average numbers of cards selected over the course of the IGT for each deck.

**Correlation analyses**

Correlation coefficient analyses were conducted to establish whether there was a relationship between depressive symptoms, EBR (striatal dopamine marker), and IGT
performance. Preliminary results indicated a significant positive relationship between depressive symptoms (CES-D scores) and IGT performance, $r=.25$, $p=.01$ (Fig. 3). A marginally significant positive relationship between EBR and IGT performance ($r=.17$, $p=.09$) was also observed (Fig. 4). The relationship between depressive symptoms and EBR was not significant, $p>.10$.

For individual deck selections, depressive symptoms were significantly negatively correlated with Deck B selections, $r=-.28$, $p<.01$, and positively correlated with Deck C selections, $r=.26$, $p<.01$. EBR did not correlate with selection of any individual decks. Table 2 shows the correlations between overall CES-D depression scores, EBR, and the proportion of each IGT deck selection.

Regression analyses

A three-step hierarchical multiple regression analysis was performed to determine whether striatal dopamine, as measured by EBR, modified the relationship between depressive symptoms and decision-making performance. CES-D depression scores and EBR were both centered at the mean for the regression analysis. In the first step, gender was added as a covariate. The results demonstrated that gender was not a significant predictor of IGT performance, $p=.31$. In the second step, we tested whether depressive symptoms and EBR independently predicted IGT performance. The results from the second-step model demonstrated that EBR and depressive symptoms significantly predicted IGT performance, $\Delta R^2=.09$, $F(3, 101)=3.69$, $p=.01$. Depressive symptoms positively predicted performance, $\beta=.23$, $p=.02$, indicating that individuals with more depressive symptomatology selected the advantageous decks more often, relative to the disadvantageous decks. Additionally, EBR was a marginally significant predictor as a single-order term, $\beta=.18$, $p=.06$, which suggests that individuals with higher $D_2$ receptor density tended to choose more advantageous IGT options. In the third step of the model, the interaction term between EBR and depressive symptoms was analyzed. The addition of this term accounted for a significant proportion of variance in decision-making performance, $\Delta R^2=.04$, $F(4, 100)=3.86$, $p=.01$, indicating that the EBR by depressive symptoms interaction significantly influenced IGT performance, $\beta=.52$, $p<.05$: Individuals who reported higher levels of depressive symptoms and who had higher $D_2$ receptor density performed better on the IGT. However,

---

3. Because approximately half of our sample met the criteria for depressive symptoms in the clinical range, we also conducted correlational analyses for participants below the CES-D cutoff and above the cutoff score of 16. In the low-symptom group, we found a marginally significant correlation between CES-D depressive symptoms and EBR, $r=.25$, $p=.09$, while the correlations between CES-D scores and IGT performance ($r=.04$, $p=.78$) and between IGT performance and EBR ($r=.07$, $p=.66$) were nonsignificant. In the high-symptom group, a significant correlation between EBR and IGT performance was observed, $r=.27$, $p=.05$. We also observed a marginally significant correlation between CES-D depressive symptoms and IGT performance, $r=.24$, $p=.07$. The association between CES-D scores and EBR was not significant in the high-depressive-symptom group, $r=.06$, $p=.65$. 

---
Table 2  Correlations between eye blink rate (EBR), depression scores (CES-D), and Iowa Gambling Task deck selections

<table>
<thead>
<tr>
<th></th>
<th>Deck A</th>
<th>Deck B</th>
<th>Deck C</th>
<th>Deck D</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBR</td>
<td>-.17</td>
<td>-.09</td>
<td>.07</td>
<td>.14</td>
</tr>
<tr>
<td>CES-D</td>
<td>.02</td>
<td>-.28*</td>
<td>.26*</td>
<td>.08</td>
</tr>
</tbody>
</table>

* Significance at the p<.01 level

Table 2 Correlations between eye blink rate (EBR), depression scores (CES-D), and Iowa Gambling Task deck selections

The main effect of CES-D depression scores and EBR from the second step were not significant in the last step of the regression, p > .10. Because some research has shown that individual difference effects only emerge in the last block of IGT trials after learning is complete (Switzer, Allen, & Kaut, 2008), we also conducted regression analyses within each of the five 20-trial blocks. These results revealed that the interaction effect between depressive symptoms and EBR on IGT performance was significant in Blocks 2 (β = .77, p = .003) and 3 (β = .55, p = .04). Figure 5 depicts the simple regression lines for the effect of CES-D depression scores on IGT performance at the mean for EBR, one standard deviation above the mean for EBR, and one standard deviation below the mean for EBR. The simple regression for the mean (β = .22, p = .02) and one standard deviation above the mean (β = .39, p < .01) significantly predicted IGT performance. The simple regression for one standard deviation below the mean, however, was not significant, p > .10.

Furthermore, three-step hierarchical multiple regressions were conducted for the proportions of selections for each of the decks individually.4 Decks A and C demonstrated differential effects of EBR and depressive symptoms. For Deck A, the first step, with gender entered as a covariate, was not a significant predictor of Deck A selections, p > .10. Similarly, the second step, with CES-D depression scores and EBR entered as single-order terms, showed no significant effects, p > .10. In the last step, however, the overall model was significant, ΔR² = .11, F(4, 100) = 4.18, p < .01. These results indicated that the EBR by depressive symptom interaction significantly influenced the selection of Deck A, β = -.91, p < .01, indicating that individuals with higher striatal dopamine D₂ receptor density and higher depression scores tended to choose Deck A less frequently. The first step of the regression for Deck C was not a significant predictor of Deck C selections, p > .10. In the second step, however, CES-D depression scores significantly predicted the frequency of Deck C selections, β = .24, p = .01. EBR was not a significant predictor, p > .10. In the last step of the model, the EBR by depressive symptoms interaction significantly predicted Deck C selections (β = .55, p = .04), and the overall model was significant, ΔR² = .04, F(4, 100) = 3.60, p < .01. These results demonstrate that depressed individuals with higher blink rates tended to choose Deck C more and Deck A less often.

Model-based analyses

All participants’ data were fit individually to each of the models described above. The fits of the models were compared using Akaike’s information criterion (AIC; Akaike, 1974). AIC values are used to compare models with varying numbers of free parameters, with the AIC penalizing models with more free parameters. For each model i, AIC is defined as:

\[ AIC_i = -2\log L_i + 2V_i, \tag{10} \]

where \( L_i \) is the maximum likelihood for model i, and \( V_i \) is the number of free parameters in the model. Smaller AIC values indicate a better fit to the data.

Overall, the VPP model fit the data best on the basis of AIC values. Table 3 shows the AIC value for each of the models. Having established that the VPP model provided the best fit to the data, we examined correlations between the best-fitting parameters from the model and self-reported overall depression scores and EBR. This uncovered a significant positive relationship between depression and the VPP model’s loss aversion parameter (λ), r = .21, p = .01. Thus, individuals with heightened depressive symptoms showed enhanced loss aversion behavior. IGT performance was also positively correlated...
Table 3  Average Akaike information criterion (AIC) value for each model

<table>
<thead>
<tr>
<th>Model</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVL delta</td>
<td>256.81 (34.73)</td>
</tr>
<tr>
<td>PVL decay</td>
<td>248.99 (38.26)</td>
</tr>
<tr>
<td>VPP model</td>
<td>242.27 (38.86)</td>
</tr>
<tr>
<td>WSLS model</td>
<td>251.54 (35.33)</td>
</tr>
<tr>
<td>Baseline model</td>
<td>266.41 (23.72)</td>
</tr>
</tbody>
</table>

Standard deviations are listed in parentheses.

with the loss aversion parameter ($\lambda$), $r=.37$, $p<.01$, suggesting that loss-aversive behavior leads to better performance on the IGT. IGT performance was also negatively related to the learning rate ($\phi$) parameter, $r=-.29$, $p<.01$, and the shape value function ($\alpha$), $r=-.40$, $p<.01$. Interestingly, EBR was positively related to the gain increment parameter ($\varepsilon_{\text{gain}}$) of the perseveration term, $r=.25$, $p=.01$, and negatively related to the decay parameter ($k$), $r=-.20$, $p=.02$. These results demonstrate that higher blink rates (i.e., higher D2 receptor density) were associated with a tendency to persevere with an option that provided net gains, thereby avoiding the options with net losses, and to discount expected values to a lesser extent than individuals with lower striatal dopamine D2 receptor density.

**Discussion**

Overall, depressive symptomatology was associated with enhanced decision-making performance on the Iowa Gambling Task. This finding is consistent with previous research by Smoski and colleagues (2008), whose work demonstrated performance advantages on the IGT in clinically depressed adults. Furthermore, on the basis of our correlational results, we did not observe a direct relationship between EBR and depressive symptoms. Instead, our results demonstrate that the interactive relationship between increased depressive symptoms and EBR influences decision-making. Thus, we found that the interaction between depressive symptoms and elevated D2 receptor density, as indexed by EBR, influences decision-making, but striatal dopamine D2 receptor density alone is not predictive of depressive symptoms. This contrasts with previous results suggesting that depression may be associated with reduced EBR (Berrios & Canagasabey, 1990; Ebert et al., 1996). However, our sample varied from those in previous studies, which may have contributed to the observed differences in results. First, the sample in the Ebert and colleagues study was composed of a small, male-only sample of participants. Several studies (Dreisbach et al., 2005; C. S. R. Li, 2006; Müller et al., 2007; Mulvihill et al., 1997), as well as the present investigation, have demonstrated that females have higher EBRs than males, on average. On the basis of these gender differences in EBR and, presumably, the underlying neurocircuitry, the results of the present investigation provide reliable findings with a large gender-representative sample that sheds light on the relationship between EBR and a broad range of depressive symptoms in both males and females. Moreover, because we observed a marginally significant correlation between high EBR and advantageous decision-making, we cannot definitively draw conclusions about the association between striatal dopamine D2 receptor availability and IGT performance. However, given the observed positive relationship, our results lend some support to previous PET work showing that increased striatal dopamine release was correlated with advantageous IGT selections (Linnet et al., 2011). Importantly, the results of this study indicate that dopamine modifies the relationship between depressive symptoms and decision-making, whereby individuals who report more depressive symptoms and have higher striatal dopamine D2 receptor density choose more advantageous deck selections on the IGT, resulting in better decision-making performance.

A more detailed examination of behavioral tendencies on the IGT from computational modeling analyses revealed that individuals with more depressive symptoms exhibited more loss-aversive behavior. These results support research showing that depressed individuals are more sensitive to losses and excel on tasks that depend on loss minimization (Beevers et al., 2013; Berenbaum & Oltmanns, 1992; Carver et al., 2008; Pizzagalli et al., 2008; Taylor Tavares et al., 2008). Additionally, individuals with high EBRs tended to persevere in choosing options that offered net gains. In line with previous research demonstrating that striatal D2 receptors regulate learning from negative feedback, the elevated D2 receptor density in depressed individuals may allow them to effectively keep track of options that offer net losses and avoid those options, and thus perform better than individuals with lower dopamine D2 receptor density.

An analysis of IGT performance by individual deck selections showed that depressive symptoms were related to decreased selection of Deck B and increased selection of Deck C, which contrasts with previous work showing that depressed individuals select Deck A more than controls, although this previous study comprised individuals with an MDD diagnosis (Cella et al., 2010). Moreover, we found that, specifically, striatal dopamine influenced the selection of Decks A (high-magnitude reward, frequent losses) and C (low-magnitude reward, frequent losses) among individuals with more depressive symptoms. Both Decks A and C gave frequent losses, but Deck A offered high-magnitude gains and losses and yielded a *net loss* over several trials, whereas Deck C provided low-magnitude gains and losses and offered a *net gain*. Therefore, although depressive symptoms may lead individuals to attend to losses, our results suggest that increased
striatal dopamine D$_2$ receptor availability in depressed individuals may also increase learning from loss/punishment frequency, which in turn may enhance identification of the options with high-frequency loss options that offer net gains. This corresponds with our results showing that individuals with elevated D$_2$ receptor availability and depressive symptoms chose Deck C more often and Deck A less frequently. From the computational modeling and individual deck analyses, we demonstrated that individuals with depressive symptoms and higher D$_2$ receptor density are better able to learn from frequent losses, thus avoiding options with net losses on the IGT and choosing the advantageous options more often.

In contrast, the interaction between striatal dopamine, as indexed by EBR, and depressive symptoms did not significantly impact Deck B and D selections. The key distinctions between Decks A and C and Decks B and D were the frequency and magnitude of losses. Decks A and C offered low-magnitude but frequent losses, whereas Decks B and D yielded high-magnitude, infrequent losses. Given that individuals with high EBR and depressive symptoms chose Deck C more and Deck A less often, we can conclude that increased attention to the expected values of options with high-frequency losses characterized their decision-making strategies. Moreover, because we observed no differences in selections of Decks B and D, the options with large, infrequent losses, it appears that striatal dopamine does not necessarily modulate sensitivity to high-magnitude rare losses in individuals with moderate depressed symptoms. This conclusion varies from those of previous work suggesting that lower spontaneous EBR is sensitive to learning from negative outcomes (Slagter et al., 2015). Several important distinctions in the procedures of Slagter et al.’s previous study and the present research may account for these differences in results. First, Slagter and colleagues used a probabilistic RL task that offered “correct” or “incorrect” feedback, whereas the task in the present study entailed positive and negative values that varied in the magnitudes and frequencies of gains and losses and provided fixed feedback. Thus, these studies varied in the formats of positive and negative feedback as well as in task complexity. We conclude that spontaneous EBR is sensitive to learning from the frequency of negative outcomes, rather than to differences in loss magnitude, and that elevated EBR in depressed individuals leads to better learning of expected values from high-frequency negative feedback. We note that our observed association between spontaneous EBR and advantageous IGT selections was marginally significant, and the central findings of this study are based on the interaction between EBR and depressive symptoms. Future work should aim at investigating differences in D$_2$ receptor functioning in depressed individuals.

Although our findings are in line with those from several previous studies, they diverge from others showing that depression is associated with disadvantageous IGT performance (Cella et al., 2010; Han et al., 2012; Must et al., 2006). Distinctions between our findings and this previous work may lie in the populations examined as well as in the measures used to assess them.

Our sample included a group of college-aged students, but previous work examining the influence of depression on IGT performance had focused on middle-aged adults ($M_{\text{age}}=35.45$ in Cella et al., 2010; $M_{\text{age}}=42.50$ in Must et al., 2006; age range=22–55 in Smoski et al., 2008) and adolescents (Han et al., 2012). To our knowledge, it appears that the young adult age group has largely been overlooked, which may contribute to the disparities between our and other studies’ findings. It is possible that age may moderate the relationship between depression and IGT performance, and future research should aim at examining this possibility.

**Limitations**

Although the results of our study provide evidence that striatal dopamine D$_2$ receptor density moderates the relationship between depressive symptoms and decisions, we note that some caveats within the study may limit our findings and should be addressed in future research. First, it is important to note that several individuals reported levels of depression that were within clinical range ($\geq 16$). Because clinical diagnostic histories of depression or other mental illnesses were not recorded, it is possible that some individuals in our sample were being treated for depression or other disorders. Therefore, future studies should control for prior clinical diagnoses and the use of psychotropic drugs, because these factors may influence dopaminergic functioning and alter spontaneous EBR. Additionally, we did not control for sleep deprivation or recent use of substances (i.e., alcohol or drugs) or stimulants (i.e., caffeine, nicotine), which could affect blink rates and might limit the implications of our results. Further work using EOG to examine depression and striatal dopamine should control for sleep and substance use. Finally, it is important to note that the depressive measure in our study considered a spectrum of depressive symptoms that had occurred in the past 7 days. Therefore, the findings of this study should be generalized to individuals experiencing recent depressive symptoms, rather than individuals who have been clinically diagnosed with MDD.

**Conclusion**

On the basis of the findings of this study, we concluded that examining how striatal dopamine interacts with such clinical disorders as depression is critical to understanding behavior in important cognitive tasks such as decision-making. Individuals often make choices that have either positive or negative consequences. For example, pursuing a desired
career, creating business plans, and investing all depend on making decisions under uncertainty that can lead to either success or failure in the short and the long term. Although depressed individuals characteristically have larger disparities between their goals and expected outcomes (Ahrens, 1987), elevated striatal dopamine D2 receptor density may allow depressed individuals to appropriately respond to decision feedback. Heightened D2 receptor density may allow for better responsiveness to feedback by updating goal representations, and thus enhancing decision-making. Thus, striatal dopamine may enhance motivation and the response to feedback in depressed individuals, resulting in a decision-making style that is characterized by identification and avoidance of options that lead to net losses. Gaining a better understanding of how neurobiological differences can interact with clinical disorders to affect cognition and behavior may ultimately advance the efficacy of the treatments that are available.

Author note: This work was supported by NIA Grant Number AG043425 to D.A.W.

References


