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Dopamine manipulations drive changes in information sampling in healthy volunteers

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Abstract

Background: Information sampling is the cognitive process of accumulating information before committing to a decision. Patients across numerous disorders show decreased information sampling relative to controls.

Aims: Here, we used the Beads and the Best Choice Tasks to study the role of dopamine (DA) signaling in information sampling.

Methods: Participants were given placebo, amisulpride or ropinirole in each session, in a double-blind cross-over design.

Results: We found that ropinirole (agonist) increased the number of beads drawn in the Beads Task specifically when participants faced a loss and decreased the rank of the chosen option in the Best Choice Task.

Conclusions: These effects are likely driven by a combination of effects at presynaptic D₂ receptors, which affect dopamine release, and post-synaptic D₂ receptors. Increased D₂ relative to D₁ activation in the striatum leads to increased sampling in the loss condition in beads. It also leads to choice of a poorer ranked option in the secretary. Decreased D₂ relative to D₁ activation leads to decreased sampling in the Beads Task in the loss condition.

Keywords

Dopamine; neural circuits; information sampling; psychopharmacology

Introduction

Information sampling refers to the behavioral process of accumulating information before making a decision. Information sampling tasks set up an explicit relationship between

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Conflict of interest

The authors declare no conflict of interest.

performance and the amount of information sampled, such that sampling more information leads to increased accuracy. Several patient groups with psychosis, behavioral addictions, or other compulsive disorders, all of which are characterized by disorders in dopamine signaling, have been shown to sample relatively little information before making choices in these tasks (Djamshidian et al., 2013; Evans et al., 2015; Huq et al., 1988; Garety et al., 1991; Dudley et al., 1997; Clark et al., 2006). Moreover, different degrees of deficiency in making informed decisions have been seen across the groups. A study comparing patients with Parkinson's Disease (PD, with and without impulsive-compulsive behaviors (ICBs)), pathological gamblers, and illicit substance abusers showed that patients with ICBs and illicit substance abusers sampled the least information (Djamshidian et al., 2012). Similar studies have shown a significant decrease in information gathering in patients with PD that have been treated with DA agonists, as opposed to levodopa (L-dopa), and in patients with schizophrenia (Djamshidian et al., 2013; Evans et al., 2015; Speechley et al., 2010; Veckenstedt et al., 2011).

The neural substrates of information sampling tasks have been examined with fMRI (Costa and Averbeck, 2015; Evans et al., 2015; Furl and Averbeck, 2011), and it has been shown that the decision to stop sampling engages a network that spans the insula, anterior cingulate and ventral striatum. In addition, participants that have sampled more information before committing to a choice have shown stronger engagement of a parieto-frontal network. However, several studies have tried to use pharmacological manipulations to affect sampling behavior, but have shown no effects. For example, participants given ketamine do not sample less information before making a decision, despite the fact that ketamine administration in healthy human participants has been proposed as a model for schizophrenia and patients with schizophrenia consistently under-draw in these tasks (Evans et al., 2012). It has also been shown that amphetamine administration does not change sampling behavior (Ermakova et al., 2014), nor does haloperidol or L-dopa (Andreou et al., 2014). Thus, previous studies have not shown effects of pharmacological manipulations in healthy human participants on drawing behavior. This is seen despite the engagement of the ventral striatum, which receives a prominent DA input (Costa and Averbeck, 2015; Evans et al., 2015; Furl and Averbeck, 2011), and the proposed role of DA in impulsivity more generally (Trifilieff and Martinez, 2014; Kohno et al., 2016).

In the present study, we manipulated dopamine by administering a D₂/D₃ receptor agonist (ropinirole), a D₂/D₃ receptor antagonist (amisulpride), and placebo, within subject in different sessions, to healthy human participants. We then tested the subjects on two information sampling tasks, to assess whether bidirectionally modulating DA has an effect on information sampling. We hypothesized that differences in information sampling tasks seen in patient groups were due to modulations activation at dopamine receptors, based on studies showing changes in sampling behavior in patients with dopamine dysregulation ((Evans et al., 2015; Averbeck et al., 2011). It is possible that previous studies that have manipulated DA signaling have not seen effects because interventions used were not as selective for D₂ receptors (Ermakova et al., 2014; Andreou et al., 2014; Sulzer et al., 2005). For this study, we chose ropinirole as the agonist because it acts by direct stimulation of DA D₂/D₃ receptors (Jost and Angersbach, 2005). As an antagonist, we chose amisulpride because, unlike previous antagonists used (e.g., haloperidol), it has less influence on both

serotonin and alpha-1 receptors (Tamminga and Gerlach, 1987). This is important because it has been shown that decreases in serotonin signaling decrease sensitivity to sampling costs in other tasks (Crockett et al., 2012).

Methods

Participants

Twenty right-handed healthy participants (17 males and 3 females) with a mean age of 36.2 ± 9.5 were selected. All participants were fluent in English, and comfortable with the tasks administered. Participants were of various origins, education levels, and backgrounds (Table 1), and were recruited using local advertising. All participants who took part in the study gave written informed consent after a full explanation of the study and procedures that would take place. All experimental procedures were approved by the Central London Research and Ethics Committee. Participants were asked to provide urine samples on each day of testing to screen for the use of cannabis, cocaine, opiates, amphetamines and benzodiazepines. All urine samples were negative for participants included in the study. Of the participants included, five were current smokers and six of the non-current smokers were former smokers. Thirteen of the participants included also reported past substance use, but all were more than six months before study. Furthermore, healthy participants were excluded if they had any previous history of mental or neurological illness, or if any first-degree relatives suffered from any previous psychotic illness. Participants were additionally excluded if they exhibited any significant visual or hearing impairment, suffered from any neurological disorder, or reported any drug dependency over the last six months.

Treatments

Healthy participants were orally administered 0.25mg of the DA D₂/D₃ receptor agonist ropinirole, 400mg of the DA D₂/D₃ antagonist amisulpride or ascorbic acid as placebo in a double-blind crossover design. The amount of ropinirole administered is the typical initial dose given to patients with Parkinson's Disease (0.25 mg with a total daily dose of 1.5-24 mg), taking into account that in healthy subjects with normal DA levels, ropinirole may produce undesirable effects at doses as low as 1 mg (Goodman et al., 2006). The amount of amisulpride was similarly chosen according to the daily dose a patient with schizophrenia would receive while avoiding undesirable side effects (200-600 mg/day) (Buschmann et al., 2007). The order of each drug administered was counterbalanced across testing days, to the extent possible, given the number of subjects. Twenty participants carried out the Beads Task, however, one subject only completed the ropinirole condition. Fifteen subjects completed the Best Choice task. However, 2 subjects did not complete the ropinirole condition. Participants completed each session with each drug as close to peak plasma concentration as possible, using an average between both drugs to preserve the double-blind. Because ropinirole has an almost complete absorption after oral administration and its bioavailability is nearly 50%, participants most likely reached peak plasma concentrations after 1.5 hours of administration (Jost and Angersbach, 2005). Amisulpride had a similar bioavailability of 48%, and has an availability peak 1 hour after oral administration (Green, 2002). Sessions were typically spaced by one week to ensure complete washout of drugs between testing sessions. The elimination half-life ($t_{1/2}$) of ropinirole was 6 hours and $t_{1/2}$

for amisulpride was 12 hours. All drugs were encapsulated and packaged by the South London and Maudsley (SLam) pharmacy and administered on the day of behavioral testing. Experimenters were told which of the drugs was administered to each patient on each occasion only after the experiment concluded, to preserve the double-blind.

Tasks - Study Design

For the behavioral tasks, participants were informed that they would be playing with fictional money (points), and that they would be paid ten pounds for completing the tasks. The order of the tasks was randomized. For the Beads Task, participants completed three trials for each of four combinations of conditions explained below (loss, no loss, 80/20, 60/40) which resulted in 12 total trials. For the Best Choice Task they completed 42 trials, 14 of each of 3 list lengths. Each task took around 10-15 minutes to complete. However, the exact amount of time taken was participant dependent, as the tasks were self-paced by pressing keys on a laptop computer.

Beads Task

Participants were given a laptop computer with the Beads Task (Fig. 1). They began with an instruction screen explaining the task prior to commencing. The experimenter confirmed that the subject understood the task and answered any questions. Subjects were asked to imagine two urns containing green and blue beads. One of the urns ("blue urn") contained mostly blue beads, while the other one ("green urn") contained mostly green beads. Subjects were told that the computer would be drawing from one of the two urns for each of the draw sequences completed. Subjects could draw up to ten times before making an urn choice. The participant's aim was to determine which of the two urns the beads were being drawn from. The number of times subjects drew during a trial was designated the "number of draws" for that trial. At the beginning of each trial, a new instruction screen came up informing the participant the ratio of colored beads for that trial (either 80/20 or 60/40) and if it was a loss (ten points) or no loss (zero points) trial for incorrect urn choice. The presence of loss in decision making tasks increases attention to choices (Lejarraga and Hertwig, 2017), and therefore we wanted to include loss to characterize its effects. Participants were always given ten points for correct choices. For each trial, subjects could press the 'b' key to choose the blue urn or 'g' key to choose the green urn when making an urn choice. Alternatively, subjects could choose to draw again by pressing the 'd' key. Each extra bead drawn resulted in a 0.20 point deduction of the total number of points earned across all trials. The color of the beads remained on the screen until an urn choice was made to reduce working memory demands.

Best Choice Task

Participants completed the Best Choice Task prior or subsequent to the Beads Task on the same laptop computer. Similar to the Beads Task, an instruction screen explaining the task was displayed prior to commencing. The experimenter confirmed that the subject understood the task and answered any questions. In this task, the participant's aim was to choose the best item from a list of either 8, 12 or 16 items. They were instructed what "feature" of the items would define its rank in the list. For example, if they were instructed to buy a car for \$10,000, the feature could be to pick the car with the lowest mileage. They were then shown

a series of cars that varied in mileage. Participants were shown options in the list, one at a time. After being presented with each option in the list, participants could either take or decline the current option. If they declined the option, they were not allowed to return to it. They were then presented with the next option. Options were ranked based on how close participants were to the best choice. Using the same example, if the options were 20K, 30K, 50K or 100K miles, and the participant chose 20K, the rank would be 1. The next two options (30K and 50K miles) would have ranks of 2 and 3, respectively. If participants took the current option, they were told its relative rank in the list and given points only if it was one of the best three options. Participants that chose list options with ranks 1, 2 or 3 would earn 5, 3 or 1 points, respectively. All declined options appeared at the bottom of the screen to reduce working memory demands. If no choice was made, and all items from the list were shown, participants were given the last option in the list.

ANOVA Analyses

The data were analyzed using mixed-effects ANOVA models. The dependent variables are indicated for each ANOVA in the results. For both tasks subject was a random effect and drug condition was a fixed effect with 3 levels for placebo, agonist or antagonist. In addition, for the Beads Task the beads ratio and loss condition were fixed effects. For the Best Choice Task list-length was a fixed effect. Although our crossover design for drug administration was beneficial to eliminate non-effect variations, it required multiple visits from each patient, which resulted in dropouts. The mixed-effects ANOVA, however, accounts for this (Kutner et al., 2005). In addition, we examined the distribution of within participant differences in draws across drug conditions, and found that they were well-modeled by a Gaussian (Lilliefors test, $p = 0.421$) and therefore the mixed effects approach is appropriate. We also examined the likelihood function for the difference in accuracy and found that it was also well approximated by a Gaussian. For the 3-way interaction on accuracy reported in the results, we had a power of 0.5 to detect the effect.

Results

Beads Task

We began by examining the behavior of participants on the Beads task (Fig. 1). We found that participants drew more in the 60/40 split than the 80/20 split (Fig. 2A; ratio, $F(1,19.2)=36.9$, $p<0.001$). This increase in draws was expected, due to bead color splits closer to chance in the 60/40 condition. Participants, however, were not affected by the loss condition (condition, $F(1,19.8)=0.8$, $p=0.389$).

However, when comparing across the three drug conditions, we found that the participant's behavior differed depending on the win-loss condition (Fig. 2A; drug*condition, $F(2,145)=3.3$, $p=0.047$). Specifically, there were main effects of drug in the loss condition (drug, $F(2,72)=7.9$, $p<0.001$) but not in the no loss condition (drug, $F(2,72)<1$, $p=0.902$). When comparing ropinirole to amisulpride, we found that participants drew more in the loss condition on ropinirole than amisulpride (drug; $F(1,36)=13.8$, $p<0.001$), but not in the no loss condition (drug; $F(1,36)<1$, $p=0.930$). After correcting for two comparisons, there were

no effects of drug in either of the ratio conditions considered individually (80/20: $F(2, 36) = 3.7$, $p = 0.033$; 60/40: $F(2, 36) = 1.1$, $p = 0.330$).

Drawing more beads improves one's ability to infer the correct urn. However, this is only true when information integration is optimal and trial-by-trial the number of beads drawn can depend on the specific sequence of beads shown. Therefore, we also examined accuracy. We found that accuracy was higher in the 80/20 split than the 60/40 split (Fig. 2B; ratio, $F(1,19.4)=37.8$, $p<0.001$). It was also, unexpectedly, higher in the no loss than the loss condition (condition, $F(1,19)=10.6$, $p=0.004$). There was a three way interaction between drug, win-loss and bead ratio (drug*condition*ratio, $F(2,145)=4.8$, $p=0.010$, $\eta^2 = 0.06$). When we compared drug effects within all conditions and ratios, however, none were significant (80/20 Loss, $F(2, 36) = 0.5$, $p = 0.635$; 60/40 Loss, $F(2, 36) = 0.1$, $p = 0.903$; 80/20 No Loss, $F(2, 36) = 0.2$, $p = 0.792$; 60/40 No Loss, $F(2, 36) = 2.6$, $p = 0.089$). We also examined correlations between accuracy and beads drawn across subjects and found a non-significant negative correlation ($\text{corr} = -0.274$, $F(1, 52) = 3.0$, $p = 0.089$).

Best Choice Task

Next, we examined the Best Choice Task (Fig. 3). We started by examining the position in the list of the chosen option, i.e. the number of options seen including the chosen option (Fig. 4A). We found that the serial position of the chosen option increased with increasing list length (list length, $F(2,29)=37.1$, $p<0.001$). There were, however, no drug effects on the serial position of the chosen option (drug, $F(2,152)=0.1$, $p=0.876$). Next, we examined the rank of the chosen option in the list. Rank refers to whether the option was the best (rank 1), second best (rank 2), etc. For all list lengths, the rank increased as the list length increased (list length, $F(2,30)=9.3$, $p=0.001$), showing that it was harder to identify the best items in longer lists, as expected. Furthermore, there was an effect of drug on the rank of the chosen option (Fig. 4B; drug, $F(2,152)=3.3$, $p=0.041$). Post-hoc comparisons showed that the rank of the chosen option was higher (i.e. the chosen option was not as good) on ropinirole than placebo (drug; $F(1,73)=6.3$, $p=0.014$), but not significantly higher on amisulpride than placebo (drug; $F(1,81)=0.1$, $p=0.813$). Finally, we correlated the mean number of draws, across subjects, in the Beads Task and the Best Choice Task and found a nonsignificant negative correlation ($r = -0.361$, $p = 0.186$).

Discussion

We examined the effects of DA manipulation in healthy controls on two tasks, the Beads Task and Best Choice Tasks. Using two tasks allowed us to ask whether the effects of dopamine on stopping would generalize across tasks, which however, differed in some aspects. We administered one pill to every participant in each session using a within-subject cross-over design. The pill was either an agonist (ropinirole), antagonist (amisulpride) or placebo (ascorbic acid) . We hypothesized that ropinirole would decrease information sampling and amisulpride would increase it. Drugs were administered in each session before behavioral testing. There were effects of DA manipulations in both tasks. We found that ropinirole increased information sampling, relative to amisulpride, in the Beads Task. We found no significant differences between placebo and either drug. However, the effects of the

drugs on dopamine receptors were in opposite directions. Therefore, comparing both drugs directly increased the effect of the manipulations, which by themselves were not strong, to show differences in sampling. We found that the rank of the chosen option in the Best Choice Task was worse on ropinirole than placebo, but the rank chosen on amisulpride did not differ from placebo.

An extensive body of research has shown that numerous patient groups sample less information than control participants in the Beads Task. For example, patients with schizophrenia, their first degree relatives, and healthy participants prone to delusional ideation, make early responses in the Beads Task (Evans et al., 2015; Freeman et al., 2008; Abi-Dargham et al., 1998; Van Dael et al., 2006; Zawadzki et al., 2012; Moutoussis et al., 2011). Under-sampling in the Beads Task has also been seen in patients with Parkinson's disease that have developed behavioral addictions, as well as pathological gamblers and opioid addicts (Djamshidian et al., 2012), and in amphetamine and opioid addicts using the box opening task, which is also a measure of information sampling (Clark et al., 2006).

Changes in DA signaling, particularly in frontal-striatal circuits, are thought to underlie or contribute to several of these disorders. Patients with schizophrenia have increased amphetamine evoked DA release in the striatum, as well as decreased release in lateral prefrontal cortex (Slifstein et al., 2015). Studies have also shown that patients with Parkinson's disease, that develop impulse control disorders, have fewer DA transporters in the ventral striatum, which likely leads to relatively elevated DA levels in that structure (Leeman and Potenza, 2011; Cilia et al., 2010). There are also numerous changes in the DA system of drug addicts, including a decrease in dopamine D₂ receptor availability in the ventral striatum (Volkow et al., 2016; Volkow and Koob, 2015). Because previous studies have found changes in dopamine signaling in patients groups, and the same patient groups also show changes in sampling behavior, it suggests that the change in sampling behavior may be due to changes in dopamine signaling. Consistent with this, functional imaging in healthy human subjects has shown that the decision to guess an urn in the Beads Task, or the decision to take the current option in the Best Choice Task, engages a network including the anterior cingulate, ventral striatum and anterior insula (Costa and Averbeck, 2015), and both the anterior cingulate and the ventral striatum receive prominent DA projections (Lewis et al., 1988; Haber et al., 2000).

Despite the data that has implicated changes in DA signaling in compulsive behaviors and schizophrenia, and their consistent performance in the Beads Task, previous attempts at changing information sampling, by pharmacologically manipulating DA signaling, have not been effective. Concerning dopamine manipulations, neither amphetamines (Ermakova et al., 2014), nor comparing haloperidol with L-dopa have shown effects (Andreou et al., 2014). In addition, administering ketamine to healthy human participants has also failed to affect sampling behavior (Evans et al., 2012). It is possible that previous studies that manipulated DA signaling did not see effects because they manipulated DA unidirectionally (Ermakova et al., 2014) or they used L-dopa to increase DA signaling (Andreou et al., 2014). L-dopa does not directly agonize post-synaptic receptors. This increase in DA signaling can be seen if there is a bottle neck in the metabolic pathway prior to the conversion of tyrosine to DOPA by tyrosine hydroxylase. Amphetamine, similarly, does not directly bind DA

receptors. Rather, it leads to decreased reuptake and reversal of the DA transporter (Sulzer et al., 2005). Thus D1 and D2 receptors will not be differentially engaged, following amphetamine administration, like they were in our study. Therefore, the most likely explanation for our results is that information sampling may be a function of the ratio between activation of the direct and indirect pathways through the striatum, which are characterized by expression of D₁ and D₂ receptors, respectively, on medium spiny neurons (Frank and O'Reilly R, 2006).

Multiple studies have analyzed the effects of loss aversion, and consistently found that there is increased attention in decision making when facing potential loss (Lejarraga and Hertwig, 2017). Also, choices in the task require assessing the impact of incorrect responses (Furl and Averbeck, 2011). Therefore, we explicitly manipulated this impact, to gain experimental control over it. It has also been shown that acute tryptophan depletion, which decreases serotonin signaling, can decrease sensitivity to sampling costs in the box opening task, in a condition where participants have to pay for additional samples (Crockett et al., 2012). Similarly, we found that the effects of drug in our study were specific to the loss condition, although we did not manipulate cost to sample.

Although we found effects of the DA manipulations on sampling behavior, data in the patient groups suggests that they are characterized by increased DA signaling relative to matched control groups, whereas we found that ropinirole, a DA agonist, led to increased sampling in the Beads Task, and amisulpride led to decreased sampling. Previous studies in probabilistic learning have seen similar reversals in the effects of DA manipulations when agonists are used in healthy human participants, relative to what is seen in patient groups (Frank and O'Reilly R, 2006). These reversals in direction of effect are likely driven by effects of the D₂ drugs on pre-synaptic D₂ auto-receptors. When these receptors bind dopamine they decrease release. Therefore, antagonizing them leads to increased dopamine release, which has been shown experimentally (Garris and Wightman, 1995). This increased release could further drive decreased sampling, since the D₁ system would be driven even harder than normal, in combination with some antagonism of post-synaptic D₂ receptors.

The Best Choice Task has not been studied, to our knowledge, in clinical populations. However, functional imaging suggests that decisions to accept an option may engage the network engaged when sampling is stopped in the Beads Task (Costa and Averbeck, 2015). Nonetheless, choices in the Best Choice Task are more complex. In the Beads Task, each bead increases the information one has about which urn is being drawn from. Individual beads, however, do not have intrinsic value, beyond the information they convey. In the Best Choice Task, each option increases the accuracy of the estimate of the probability distribution from which one is sampling, and the option has intrinsic value. It can be accepted or rejected on the basis of its value. Thus, the aspects of the formal decision mechanisms underlying performance in these tasks differ, although both tasks are optimal stopping problems. We had hypothesized that the stopping mechanism might be general across tasks and therefore might be affected similarly by drug. However, we did not find consistent results.

We have previously fit ideal observer models to both tasks. These models generate optimal behavior. In the Beads Task, one should continue to sample, until the expected value of guessing the most probable urn color is higher than the expected value of guessing after sampling additional beads (Furl and Averbeck, 2011). Because there is a charge for beads, it is not optimal to sample all 10 beads. The Best Choice Task is more complex. As one samples options, one builds up an estimate of the distribution over samples. Each option can then be compared to this distribution. The probability of sampling a better option can then be calculated, given the remaining number of samples, and the estimated distribution. Given this information, one can calculate the value of accepting the current option, or continuing to sample. Both tasks are optimal stopping tasks, and the choice to stop sampling in both tasks engages a similar network of brain areas. In both tasks, the choice to stop is a choice between accepting the value of an option now, and delaying reward (or loss) until the future. Therefore, they share underlying computational and neural features. Unfortunately, the results in the two tasks are not easily integrated. Although the computational and systems level neural aspects of the tasks are similar, they responded in ways that are difficult to relate, under drug administration.

Limitations of the study need to be acknowledged. Low doses of amisulpride are known to enhance DA transmission by preferentially blocking presynaptic D₂/D₃ DA receptors, while higher doses inhibit transmission by blocking postsynaptic receptors (Rosenzweig et al., 2002). More precise measurements of drug plasma levels could explain if increased DA is associated with drawing of more beads in healthy controls, like we saw in our results, or if DA transmission changed direction, or did not even reach the level needed for the direction we expected. Another possible limitation is that we lack sufficient information to know if past drug use of any of the participants had a long lasting effect on their behavior. Finally, the ceiling effect on accuracy in the 80/20 condition limits our ability to see drug effects in this condition.

Conclusions

We found effects of manipulating signaling at DA D₂/D₃ receptors on two information sampling tasks. Ropinirole increased draws relative to amisulpride in the Beads Task, and increased the rank of the chosen option in the Best Choice Task. These behavioral changes were likely driven by drug effects at pre-synaptic auto-receptors, as patient groups with increased DA signaling have previously been shown to draw less on the Beads Task. This study, therefore, increases the evidence in favor of a role for DA signaling in driving evidence accumulation in information sampling problems. Future research will be necessary to pin down the effect of individual variability in DA signaling within specific brain circuits on sampling behavior, to further elucidate the mechanisms underlying this behavioral process. Studying broader functions of DA with these tasks could provide further insight into the participant's decisions. For example, the relationship between increased extracellular DA and the valuation of novel stimuli in decision making (Costa et al., 2014), gambling (Rutledge et al., 2015; Rigoli et al., 2016), addiction (Spinella, 2003), or risky behavior (Rutledge et al., 2016) could be closely linked to participants' sensitivity to the value of the chosen option. Understanding normal variability in sampling behavior and the

brain circuits that underlie this behavior may further generate insight into pathology in neural circuits in groups that show aberrant sampling on these tasks.

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Figure 1-

Beads Task design. Subjects were shown an instruction screen indicating the ratio (i.e. 60/40 or 80/20) of beads in the urn and if it was a loss or no loss trial. After 2.5 s, subjects were shown the first bead. They could then draw another bead (incurring a 0.20 point deduction) or choose the urn (blue or green) they thought the beads were being drawn from. Subjects who chose an urn were shown a feedback screen informing them if they had chosen the correct urn (blue in the example; subject won 10 points) or not (subject lost 10 points). Subjects who did not choose an urn and decided to draw again could draw up to 10 beads before having to make a decision.

Figure 2 –.

Effect of drug on behavioral performance (A) Mean draws of participants administered placebo, ropinirole or amisulpride during trials with a probability ratio of 80/20 or 60/40 in the loss and no loss conditions. Error bars are standard error of the mean (s.e.m.) across subjects for each condition, where $n=19$ for participants on placebo and amisulpride and $n=20$ for participants who received ropinirole. (B) Mean accuracy of urn choice in healthy participants.

Figure 3-

Best Choice Task. Subjects were shown an instruction screen informing them of the list length for that trial (8, 12 or 16). After 6 s, subjects were presented the first option in the list. Subjects could either decide to take the item or see the next one from the list. If subjects decided to see the next item, they could not go back to a previous item. Subjects could win either 1, 3 or 5 points if they chose one of the top three ranked objects, where a higher rank corresponded to more points (i.e. rank 1 was 5 points). No points were earned for any other object chosen with a lower rank.

Figure 4 –.

Effect of drug in healthy participants on behavioral performance (A) Mean position in list of chosen option for participants administered placebo, ropinirole or amisulpride during trials of lists 8, 12 or 16 options long. Error bars are standard error of the mean (s.e.m.) across subjects for each list length, where $n=15$ for participants on placebo and amisulpride and $n=13$ for participants who received ropinirole. (B) Mean absolute rank of chosen option in healthy participants.

Table 1-

Demographic characteristics. This study is a component of a larger study that includes patients with schizophrenia. To match that sample, we have included mostly males. We also matched smoking habits with the patient group. All values are mean $\pm$ standard deviation. DSST= Digit symbol substitution test.

Participants (no.)	20
Age (years)	36.2 $\pm$ 9.5
Gender (female)	3
Current smokers (years)	4.1 $\pm$ 8.1
Cigarettes-current (day)	9.0 $\pm$ 6.4
Former smokers (years)	1.6 $\pm$ 4.8
Cigarettes-former (day)	8.2 $\pm$ 7.3
Alcohol users (units)	6.1 $\pm$ 6.3
Right-handed (no.)	20
English-First Language (no.)	19
Fluency in English (no.)	20
Education (years)	15.3 $\pm$ 2.4
NS-SEC	2.4 $\pm$ 1.6
Raw Vocabulary (WASI)	61.7 $\pm$ 8.5
Raw Matrix (WASI)	25.9 $\pm$ 4.8
IQ (WASI)	107.8 $\pm$ 14.3
Raw/50 (NART)	31.2 $\pm$ 6.4
IQ (NART)	76.9 $\pm$ 12.9
DSST	55.5 $\pm$ 10.2
Amphetamines (no.)	8
Cannabis (no.)	12
Cocaine (no.)	7
Benzodiazepines (no.)	1
Opiates (no.)	1