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Separate neural substrates for skill learning and performance in the ventral and dorsal striatum

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It is widely accepted that the striatum of the basal ganglia is a primary substrate for the learning and performance of skills. We provide evidence that two regions of the rat striatum, ventral and dorsal, play distinct roles in instrumental conditioning (skill learning), with the ventral striatum being critical for learning and the dorsal striatum being important for performance but, notably, not for learning. This implies an actor (dorsal) versus director (ventral) division of labor, which is a new variant of the widely discussed actor-critic architecture. Our results also imply that the successful performance of a skill can ultimately result in its establishment as a habit outside the basal ganglia.

There is extensive evidence that both the ventral and dorsal striatum are involved in instrumental conditioning[1–10]. However, it remains unclear what the precise relationship is between these two striatal areas. Original anatomical studies described each of the two areas as part of distinct and closed corticostriatal loops. The ventral striatum connects to the ventral prefrontal cortices (for example, the orbitofrontal cortex), whereas the dorsal parts of the striatum connect to the dorsal prefrontal and motor cortices[11]. However, new evidence suggests that there may be a number of pathways by which the different cortico-striatal loops can interact[12,13]. Also, functional studies have shown that both areas are involved under the same task demands. For example, functional magnetic resonance imaging studies have shown that both the ventral and dorsal striatum are active during instrumental learning[10,14]. Similarly, lesions of both the ventral[15] and dorsal[6] striatum impair performance on the instrumental lever-pressing task. In this paper, we provide direct evidence in the same experimental paradigm that the dorsal striatum is strictly responsible for performance and not learning, whereas the ventral striatum is involved in both learning and performance of skills. Also, we found that correct performance expressed by the dorsal striatum can ultimately result in a skill becoming independent of the basal ganglia. Taken together, those results warrant a new actor-director model of basal ganglia function that is a variation of the widely debated actor-critic architecture[16]. Thus, we argue that initial learning in the ventral striatum (director) guides the dorsal striatum (actor) to express an instrumental response. Ultimately, the consistent expression of the instrumental response results in a learning process that establishes the habit outside the basal ganglia[17].

We trained rats on a two-alternative forced choice task (A+B–) using a Y-maze apparatus, with correct choices determined by olfactory cues. Intact rats achieve high levels of performance on this task within three 20-trial training sessions (S1, S2 and S3). We made a matched set of reversible manipulations to the ventral and dorsal striatum during acquisition (before each of the three training sessions) and in a subsequent test session (S4) using the $GABA_A$ agonist muscimol (which temporarily inhibits neural firing) and the NMDA antagonist AP-5 (which temporarily blocks a dominant form of synaptic plasticity). If the ventral striatum is critical for learning and performance, muscimol injections during the acquisition phase should have lasting effects on test performance. In other words, if the rats do not acquire the contingency between stimulus and response during the acquisition phase, they should be impaired in the test phase even if they are drug free during that test. Also, muscimol should impair performance when injected during the test phase. Furthermore, AP-5 should also block learning, but not test performance.

If the dorsal striatum is critical for performance but not learning, muscimol injections during the acquisition phase should impair performance, but if muscimol is omitted during test, performance should recover to control levels. Furthermore, AP-5 should have no effect. This is exactly the pattern we found.

RESULTS

Experiment 1

In the first experiment, we tested four groups with cannulas in the ventral striatum (primarily the core of the nucleus accumbens; see **Supplementary Figs. 1** and **2** online for cannula locations): rats in the MUSacq group received a muscimol injection before each session in the acquisition phase (a total of three injections); rats in the MUStest group received an injection before the test phase only; rats in the AP-5acq group received an AP-5 injection before each session on the acquisition phase; and rats in the AP-5test group received an AP-5 injection before the test phase.

Muscimol injections in the ventral striatum impaired the acquisition of the instrumental response, because there was no recovery of

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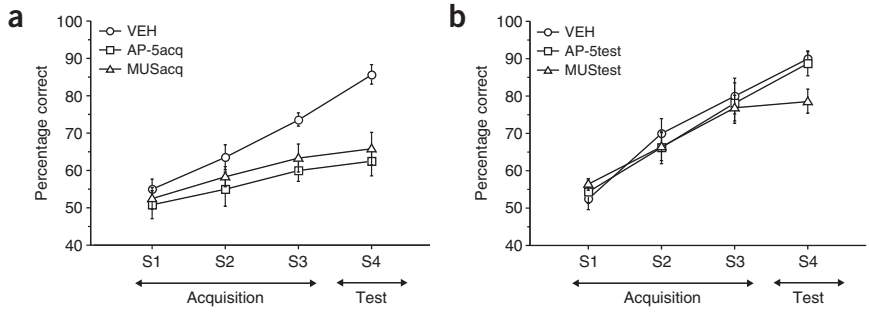

Figure 1 Effects of muscimol and AP-5 in the ventral striatum on the instrumental task. (**a**) The effect of vehicle ($n = 7$), muscimol ($n = 6$) or AP-5 ($n = 6$) injections in the ventral striatum during the acquisition phase (S1, S2 and S3). Both muscimol (GABA agonist) and AP-5 (NMDA antagonist) impaired the acquisition of the task (**b**) Effect of vehicle ($n = 8$), muscimol ($n = 11$) or AP-5 ($n = 8$) injected in the ventral striatum on the test phase (S4) of the instrumental task. Muscimol caused a mild impairment on performance, whereas AP-5 had no effect. In this and all subsequent graphs, error bars represent the s.e.m.

performance in the final test phase (**Fig. 1a**). A Bonferroni *post hoc* test showed a significant difference between the MUSacq group and the vehicle-only VEH group during the test phase ($P = 0.0012$). This conclusion was further supported by data from the AP-5acq group, which also showed acquisition deficits relative to the VEH group on the test phase ($P = 0.0003$). Although this drug produced longer-latency responses (**Fig. 2a**), AP-5 injections only at test (AP-5test) produced no impairment in performance (**Fig. 1b**) relative to the VEH group ($P = 0.79$) even though this drug produced longer latency responses (**Fig. 2**). Thus, it is clear that the AP-5acq effects are not attributable to a performance effect. In contrast, muscimol injections at test (MUStest) caused a significant impairment of performance ($P = 0.013$) (**Fig. 1b**).

Experiment 2

In this experiment, we repeated the same manipulations in the dorsal striatum. The only addition was a MUSacq+test group that received muscimol injection before both the acquisition and the test phases (a total of four injections).

The overall pattern of results clearly showed that the dorsal striatum was critical for performance, but not acquisition, of instrumental conditioned responses. Muscimol impaired performance whether injected during the acquisition phase or the test phase (**Fig. 3**). A Bonferroni *post hoc* test showed that the MUSacq+test group performed significantly worse than both the VEH group ($P < 0.0001$) and the MUSacq group ($P < 0.0001$) on the test phase (**Fig. 3a**). Also, the injection of muscimol during the test phase only (MUStest) caused a significant impairment ($P = 0.0096$) (**Fig. 3b**). The reversible lesion technique enabled us to determine that dorsal striatum, unlike the ventral striatum, did not play a role in acquisition. This scenario was clearly demonstrated by the recovery of the MUSacq group on the test phase (S4). The performance of the MUSacq group increased from 54% correct on S3 to 83% on S4 (**Fig. 3a**). There was only a marginally significant difference between the MUSacq and VEH ($P = 0.015$). This recovery was not due to new learning in the test phase, because the performance of the MUSacq group on the first five trials of the test phase was identical to the performance of controls (**Fig. 4a**). We also tested the MUSacq+per group in a fifth session to replicate the effect found in the MUSacq group on the test phase (**Fig. 4b**). This group showed a similar recovery in performance (mean, 79%; s.e.m., 4.3%). Also, the inability to express the conditioned response was not due to a gross motor impairment, because muscimol did not affect response latencies (**Fig. 2b**). The absence of a significant deficit in the AP-5acq group ($P = 0.87$) is also consistent with the view that the dorsal striatum is not involved in the acquisition of the instrumental response (**Fig. 3a**). As a whole, the results imply that the dorsal striatum is involved in the expression but not the acquisition of the information needed in this task.

Experiment 3

Our results were consistent with the hypothesis that different areas of the striatum are involved in supporting the acquisition and expression of an instrumental choice response. It is possible, however, that the rat's choice behavior in our task is not controlled by the instrumental contingencies of the task (that is, an association between a stimulus and a response). Instead, the rat might have just associated the two odors with the different outcomes: A–reward and B–no reward (that is, pavlovian conditioning). It would then approach the odor associated with food. This hypothesis predicts that simply exposing the rats to the A–reward and B–no reward relationships should be sufficient to generate the correct response. To test this hypothesis, rats were simply placed in the goal boxes containing different odors and given food or no food (pavlovian pretraining). They were then transferred to the standard instrumental version of the task where they had to make a choice between the two stimuli. During the pavlovian pretraining, rats were either exposed to the same (A+B–) odor-reward relationship that was used in the test or to different odors (X+Y–). If odor-reward associations mediated the rats' choice behavior, then one would expect that rats in the A+B– condition would display enhanced performance when transferred to the instrumental version of the task. To measure any transfer from pavlovian pretraining to instrumental conditioning, we analyzed performance on the first five trials of the instrumental task. An unpaired *t*-test showed no significant difference between the A+B– group (mean, 55%) and the X+Y– group (mean, 50%), $t_{14} = 0.51$, $P = 0.62$ (**Fig. 5** inset). A one-sample *t*-test showed that the performance of the A+B– group was not significantly different from chance

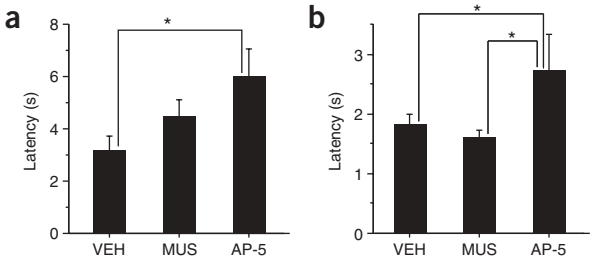

Figure 2 Response latencies (seconds) after injections in the ventral and dorsal striatum. (**a**) In the ventral striatum, a one-way ANOVA showed a main effect of drug, $F_{2,45} = 3.27$, $P = 0.047$. A Bonferroni *post hoc* analysis showed that AP-5 delayed response latencies relative to the VEH groups ($P = 0.014$). In contrast, there was no significant difference between the latencies of the VEH and MUS groups ($P = 0.25$). (**b**) A one-way ANOVA showed a main effect of drug in the dorsal striatum, $F_{2,23} = 3.91$, $P = 0.035$. A Bonferroni *post hoc* analysis showed that the AP-5 delayed the response latencies relative to both the VEH groups ($P = 0.029$) and the MUS groups ($P = 0.013$). However, there was no statistical difference between the MUS and VEH groups ($P = 0.48$). *$P < 0.05$.

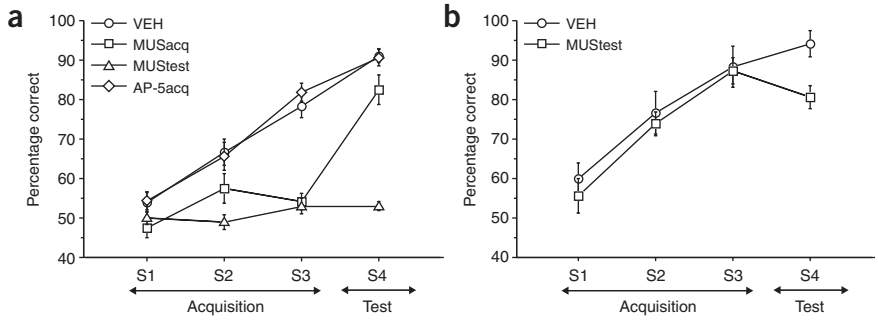

Figure 3 Effects of muscimol and AP-5 in the dorsal striatum on the instrumental task. (**a**) The effect of vehicle, muscimol or AP-5 injected during the acquisition phase (S1–S3) of the instrumental task (with the exception of the MUSacq+test group, which received injections on both the acquisition and test phases). Both the MUSacq ($n = 6$) and the MUSacq+test ($n = 5$) groups were impaired relative to the controls ($n = 9$). Yet the MUSacq group showed a substantial recovery on the test phase (no injection). In contrast, AP-5 ($n = 8$) had no effect on the acquisition of the task. (**b**) Effect of vehicle ($n = 6$) or muscimol ($n = 9$) injected in the test phase (S4). The muscimol injection resulted in a mild impairment on the test phase.

performance (50%) ($P = 0.56$). Additional training on the A+B– instrumental task also produced no difference between the two groups (repeated-measures ANOVA, $F_{1,14} = 0.15$, $P = 0.70$) (**Fig. 5**).

We also tested two additional groups for preference of the rewarded and unrewarded stimuli to show that the pavlovian pretraining was effective in establishing a stimulus-reward association. The training procedure was identical to the one described above. After training, we assessed the effect of pretraining by placing the rats in the box containing either the A or B odor and determining the time it took the rat to exit the box. Rats in the A+B– condition showed clearly that they had learned the odor-reward contingency, because they took much longer to exit the box containing the A odor than the one containing the B odor. In contrast, rats in the X+Y– condition spent, if anything, more time in the box containing the B odor (**Fig. 6**). A repeated-measures ANOVA with time difference as the dependent measure (Time A – Time B) showed a significant group difference, $F_{1,12} = 14.1$, $P = 0.0027$.

Thus, the pavlovian pretraining procedure was successful is establishing an odor-reward association, but this association was not enough to support performance on the instrumental task. The ability of pavlovian clues to enhance instrumental response has been demonstrated before[18,19]. Yet a number of factors may explain the absence of such transfer in the current experiment. First, we used choice instead of rate of response as a measure of instrumental conditioning. Second, every correct response was followed by reward as well as by the conditioned cue. Thus, the availability of the natural reward may have saturated the reinforcement process to the extent that the addition of a conditioned cue had no noticeable impact.

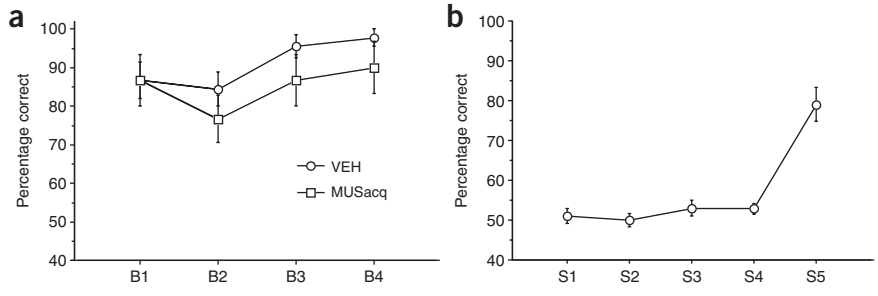

Figure 4 The effect of muscimol in dorsal striatum on subsequent test performance. (**a**) A repeated-measures ANOVA on the performance of the MUSacq and VEH groups on the test phase (S4) subdivided into four blocks of five trials each showed a significant block effect ($P = 0.049$) but no significant group effect (MUSacq versus VEH) ($P = 0.12$). In addition, there was no significant interaction between the block and group variables ($P = 0.79$). The performance of both groups was identical on the first block of trials (mean, 87%). (**b**) Performance of the MUSacq+test group when tested drug-free on a fifth session (S5). Bonferroni *post hoc* tests showed that performance was superior on S5 relative to all the previous sessions ($P < 0.0001$). Also, none of the first four sessions were significantly different from one another ($P > 0.1$).

DISCUSSION

These results show that the dorsal and ventral striatum take on different roles in an instrumental conditioning task. The dorsal striatum is responsible for performance but not learning, and the ventral is responsible for both learning and performance. The performance deficits are consistent with the effects of permanent lesion of the dorsal striatum[1,3,6], but the reversible lesion technique showed that the dorsal striatum, unlike the ventral striatum, was not playing a role in acquisition. Even though this study showed for the first time a clear dissociation between the acquisition and expression of an instrumental task, some indication of this dissociation is present in the rodent literature[9,20–22].

Two experiments[9,20] have shown that plasticity in the dorsal striatum may even be detrimental to instrumental conditioning. The injection of a protein synthesis inhibitor in the dorsal striatum increases the rate of lever-pressing for food. The same manipulation in the core of the nucleus accumbens impairs the acquisition of the response[9]. Similarly, the expression of a plasticity-related immediate-early gene in the dorsal striatum correlates negatively with the number of lever presses[20]. This pattern suggests that dorsal striatal plasticity has a function that is incompatible with instrumental conditioning.

Evidence from human and nonhuman primates points to a similar distinction between ventral and dorsal striatum[10,14,23,24]. In addition, the medial caudate nucleus in primates displays similar properties to those of the ventral striatum. This is not surprising given that both the ventral striatum and the medial caudate receive similar projections from cortical areas known to process reward information[11,13]. For example, functional magnetic resonance signal in both the ventral striatum and the caudate nucleus correlates with the reward prediction error[10,23–27]. The reward prediction error, which is a measure of the mismatch between the expectancy and availability of reward, is believed to be tightly linked to learning[16,28]. Similarly, neuronal firing in the caudate is attenuated when a monkey reaches maximal performance[5,29].

In contrast, activity in the dorsal putamen correlates with measures of performance but not of learning[5,14,23,29]. For example, the number of neurons that fire just before the execution of a response is larger in the putamen than the caudate[5,29]. Also, unlike activity in the caudate, that in the putamen is at its highest when the subject reaches maximal performance[5,29]. This functional evidence

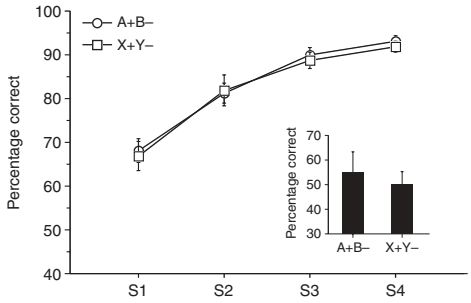

Figure 5 The effect of pavlovian pretraining on instrumental performance. This graph shows the performance of the A+B– ($n = 8$) and X+Y– ($n = 8$) groups on the instrumental task after they completed the pavlovian pretraining. There was no significant difference between the two groups. Inset: performance of the two groups was also similar on the first five trials of the instrumental task.

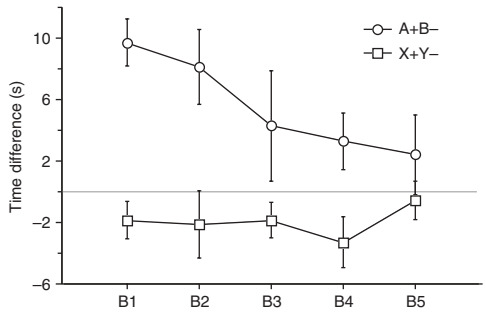

Figure 6 The effect of pavlovian pretraining on a pavlovian test. The *y* axis represents the difference in time spent in stimulus A and stimulus B. The *x* axis represents consecutive blocks of trials (two trials each). The A+B– group ($n = 7$) showed a larger time difference than the X+Y– group ($n = 7$). A repeated-measures ANOVA showed a significant group effect ($F_{1,12} = 14.1$, $P = 0.0027$) but no significant block effect ($P = 0.15$) or interaction between group and block ($P = 0.1$). One-sample *t*-tests showed that the time difference of the A+B– group was significantly above zero ($P < 0.0001$), whereas that of the X+Y– group was below zero ($P = 0.0062$).

and anatomical evidence from the rodent[30,31] indicate that the dorsal striatal area targeted in our study may be equivalent to the primate dorsal putamen.

It is notable that the expression of the instrumental response was completely blocked when muscimol was injected into the dorsal striatum prior to each acquisition session (**Fig. 3a**). Thus, we found it surprising that muscimol had only a small effect on performance when it was injected after rats had correctly expressed the task (**Fig. 3b**). One possible explanation for this discrepancy is that the consistent expression of the instrumental response results in a consolidation process of the stimulus-response association in an extrastriatal brain area. A simple Hebbian process in the cerebral cortex can result in the association of a stimulus and response that are consistently correlated, independently of the feedback-driven reinforcement process that is supported by the basal ganglia[17,32,33]. In other words, the basal ganglia can 'fix' the relationship between the stimulus and response in cortex. Consistent with that idea, one recent study reported that learning-related changes in cortical neuronal activity lag behind changes in the striatum[34].

Given that instrumental behavior is initially goal directed and later becomes habit driven[35,36], a reasonable conclusion is that the basal ganglia are not part of the habit system but make an important contribution to goal-directed behavior. Further investigation is needed to establish the extent to which behavior is goal directed or habit driven in our task. This issue is also relevant to the interpretation of our results in the context of the actor-critic model that is associated with habit-driven learning[37].

An alternative view is that the dorsomedial striatum supports goal-directed behavior whereas the dorsolateral striatum supports habit-driven behavior[38–40]. Our injection site was in the central part of the dorsal striatum (see **Supplementary Figs. 3** and **4** online for cannula locations). Thus, it is likely that both the dorsomedial and dorsolateral parts of the striatum were disrupted, which implies that an extrastriatal brain region supported test performance.

At a theoretical level, these results indicate an actor-director-critic architecture in the striatum, as contrasted with the widely discussed actor-critic architecture[16,41]. In the actor-critic architecture, the critic drives learning in the actor, which actually performs the actions that lead to reward. According to our data, the dorsal striatum only partially conforms to this actor role. It is involved in the performance of actions but plays no role in learning them. Additionally, the ventral striatum acts more like a director than a critic: it somehow learns the relevant task demands and directs the dorsal striatum to perform the appropriate action plans, but, crucially, it does not train the dorsal striatum. Given that dopaminergic inputs from the ventral tegmental area and the substantia nigra play the role of the critic[28,42], our data suggest that there is a director system that possibly mediates the effect of the critic on the actor.

We suggest two ways the ventral striatum might direct the dorsal striatum. It could modulate the activity in the orbitofrontal cortex[43] that maintains representation of the task-relevant reward contingencies. These reward representations can exert top-down control on the dorsal striatum to bias the selection of a certain response[43–45]. Alternatively, ventral striatum might do this by exerting modulatory control over the dopaminergic projections to dorsal striatum. The ventral striatum sends projections to the substantia nigra, which in turn sends projections to the dorsal striatum[12,46]. Future research is needed to test these and other possible mechanisms.

METHODS

Subjects. One hundred nineteen adult male Long-Evans rats weighing 250–300 g at the start of the experiments were bred at the University of Colorado. Rats were housed in pairs in plastic cages with *ad libitum* access to water, maintained on a 12-h light-dark cycle and given 1 week to acclimate to colony conditions before experimentation began. Access to food was restricted to maintain the rats at 80% of their free-feeding weights. To maintain that weight, rats were fed 10–15 g of rat chow after each daily training session. We conducted all experiments in accordance with protocols approved by the University of Colorado Animal Care and Use Committee.

Surgery. Under halothane anesthesia, we placed rats into a stereotaxic apparatus (David Kopf Instruments) and implanted 26-gauge stainless-steel guide cannulas (Plastics One) bilaterally into the ventral striatum or dorsal striatum. Based on the rat brain atlas[47], we used the following coordinates relative to bregma for bilateral implantation in ventral striatum: anteroposterior, +1.5 mm; mediolateral, ±2.1 mm; dorsoventral, –6 mm. We used the following coordinates for bilateral implantation in dorsal striatum: anteroposterior, +0.5 mm; mediolateral, ±3.0 mm; dorsoventral, –3.6 mm. We fixed cannulas to the skull with dental acrylic and three small screws. To maintain patency, after surgery we placed an obturator into the guide cannula that extended 1 mm in the ventral striatum and 0.5 mm in the dorsal striatum beyond the tip of the guide cannula. Rats were allowed to recover for 7 d before being trained on the behavioral task.

Apparatus. We trained the rats in a Y-shaped plexiglass maze. It consisted of a narrow runway (40 × 10 × 11 cm) that led to a gradually widening space (maximum width 32 cm). Two identical plastic boxes (25 × 10 × 32 cm) were

placed side by side in that space. The position of each box (that is, left or right side) was interchangeable on a trial-by-trial basis. A specific mix of a food spice and construction sand (100 g, Quickrete No.1961) was spread out across the whole floor of each box. One box contained a mix of cumin powder (McCormick) and sand at a concentration of 0.17 g of cumin per 100 g of sand. The other box contained a mix of cocoa powder (Hershey) and sand at a concentration of 2 g of cocoa per 100 g of sand. We selected those concentrations to equate odor intensity, which was subjectively evaluated by the experimenter. We replaced the sand-spice mixes frequently to remove contaminants (for example, food reward residue). Each box had a small opening (7 × 5 cm) at a rat's head level on each side to increase the rat's opportunity to sample both spices before entering one of the boxes. If the rat entered the 'correct' box, we manually delivered half a piece of Froot Rings breakfast cereal (Kroger) through a hole in the top of the box. The placement of the hole resulted in the food falling at the farthest end of the box. Between trials, we placed the rats in a plastic holding container located near the Y-maze.

Behavioral procedure. *Habituation phase.* At the beginning of the experiment, we placed the rats in the apparatus excluding the boxes. We placed food pieces randomly across the maze before introducing the rats to the apparatus. When the rats started to consistently and rapidly consume the food, we introduced the two boxes, but without the spice-sand mix. At this point, the food was placed inside the boxes only. The habituation period ended when each rat had run for at least ten consecutive trials with the food delivered only after the rat had entered either of the two boxes. After completion of the habituation phase, the rats underwent surgery for cannula installation. One week after surgery, the acquisition phase started for rats in experiment 1 and 2. In experiment 3, rats were not operated on. They immediately underwent the pretraining phase.

Pretraining phase. In experiment 3 only, rats received three sessions of pavlovian pretraining after the habituation phase. In this phase, we exposed rats to the stimuli by placing them in the boxes. The sequence of trials was yoked to the behavior of the control rats in experiment 1. Each rat in experiment 3 was associated with a control rat from experiment 1. For example, if on a specific trial a control rat made an approach to stimulus A+, we placed his yoked associate in experiment 3 in the box containing stimulus A+. In both cases, we provided the rat with a reward. Thus, the pretraining phase in experiment 3 was identical to the training phase in experiment 1 except that the rats did not have to perform any responses to receive the reward. Two groups went through the pretraining phase. We rewarded the A+B– group in the presence of cocoa (A+) and not in the presence of cumin (B–). We rewarded the X+Y– group in the presence of basil (X+) and not in the presence of celery (Y–).

Acquisition phase. The acquisition phase consisted of a daily session of 20 trials for three consecutive days (a total of 60 trials). All groups went through this phase. A trial started with carrying the rat from the holding container and releasing it at the beginning of the runway. If the rat entered the box containing cocoa (stimulus A+), we rewarded the rat with half a piece of food dropped inside the box. We also recorded a 'correct response' for that trial. In contrast, if the rat entered the box containing cumin (stimulus B–), no reward was delivered inside that box. Instead, we removed the rat from the B– box and placed it in the A+ box, where it was allowed to consume a half a piece of food. In this case, we recorded an 'incorrect response' for that trial. We recorded an entry as a response when all four limbs of the rat were inside the box. After the rat consumed the food, we returned it to the holding container and reconfigured the boxes for the next trial. The A+ and B– boxes were equally likely to be placed on the left or right side according to a pseudorandom sequence. For each session, we measured performance as the percentage of correct trials. In addition, we measured the latency of each trial, which was the time elapsed from releasing the rat in the runway to an entry in one of the boxes.

Test phase. The test phase occurred on the day after the acquisition phase was completed. It consisted of a single session of 20 trials using the exact same behavioral procedure as above. The only procedural difference between the acquisition and test phases was in the pattern of injections. Groups that received injections during the acquisition phase were not injected in the test phase and vice versa (see the Microinjections section for more detail).

Pavlovian test. Two groups (A+B– and X+Y–) that received the pavlovian pretraining went through a pavlovian test. We placed them in the box containing either the A or B odor with no reward available. We measured the time it took the rat to exit the box (half the body outside the box). We presented each stimulus ten times (pseudorandomly interleaved). The identity of the first stimulus to be presented was counterbalanced across rats.

Microinjections. We gently wrapped the rat in a soft towel, removed the obturator and inserted a 33 gauge microinjector (Plastics One) attached to polyethylene 50 (PE50) tubing through the indwelling guide cannula. The distal end of the PE50 tubing was attached to a 100-µl (Hamilton) syringe that was attached to a microinjection unit (model 5000; David Kopf Instruments) that accurately dispensed the desired volume. The microinjectors extended 1 mm and 0.5 mm into ventral striatum and dorsal striatum respectively beyond the tip of the guide cannulas.

As mentioned above, for each drug, we divided rats into an acquisition and a test group. The acquisition groups received either a vehicle or a drug injection before each daily session of the acquisition phase (a total of three injections). Those rats were not injected for the fourth session (the test phase). In contrast, the test groups were not injected for the acquisition phase. They received a single drug or vehicle injection before the test phase.

Drugs. Muscimol, a GABA agonist provided by Sigma in powder form, was dissolved in a saline solution. For injections in the ventral striatum, we used a muscimol concentration of 0.125 µg µl^{-1}, injecting 0.5 µl in 2 min for a total of 63 ng per side. We tested the rats immediately after the injection. For injections in the dorsal striatum, we used a concentration of 0.25 µg µl^{-1}, injecting 0.6 µl in 2.5 min for a total of 156 ng per side. We left the microinjectors in place for an extra 1.5 min and tested the rats 15 min after the injection. For both groups, control rats received a saline vehicle injection using the same parameters as their respective groups.

D-AP-5, an NMDA antagonist provided by Tocris in powder form, was dissolved in a saline solution. For injections in the ventral striatum, we used a concentration of 2 µg µl^{-1}, injecting 0.5 µl in 2 min for a total of 1 µg per side. For injections in the dorsal striatum, we used a concentration of 5 µg µl^{-1}, injecting 0.6 µl in 2.5 min for a total of 3 µg per side. We left the injector in place for an extra 1 min and tested the rats immediately thereafter. Control rats received a saline vehicle injection using the same parameters as their respective groups.

Histology. At the completion of the experiment, we anesthetized rats with pentobarbital (50 mg per kg body weight), decapitated them, removed their brains and froze the brains in cold isopentane. We cut coronal sections (40 µm thick) through the striatum with a cryostat at –19 °C and mounted every third section. We stained sections with cresyl violet and examined them by light microscopy to visually verify the placement of the cannulas. Only rats with proper cannula placements were included in the analyses of each experiment (see **Supplementary Fig. 1** for placement data).

Statistics. We used four separate repeated-measures ANOVAs to analyze the performance data. Each analysis included data from one brain area (ventral or dorsal striatum) and one injection pattern (during acquisition or during test phase). The reason was that the performances of control rats (VEH) in those conditions were not identical to one another. An analysis of the VEH groups across the four sessions showed that rats injected with saline during the acquisition phase (three injections) performed worse than those injected on the test phase (one injection) ($P = 0.039$). In addition, VEH rats with cannulas in the ventral striatum performed marginally worse than rats with cannulas in the dorsal striatum ($P = 0.065$).

Subsequently, Bonferroni *post hoc* analyses were performed for a specific number of planned comparisons. In order to protect against an inflated type I error due to multiple comparisons, we used the Bonferroni correction method to adjust our α values. For each analysis, we computed a new α (dividing 0.05 by the number of planned comparisons).

Note: Supplementary information is available on the Nature Neuroscience website.

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COMPETING INTERESTS STATEMENT
The authors declare that they have no competing financial interests.

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