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Dorsal Striatum Mediates Deliberate Decision Making, Not Late-Stage, Stimulus–Response Learning

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Abstract: We investigated a controversy regarding the role of the dorsal striatum (DS) in deliberate decision-making versus late-stage, stimulus–response learning to the point of automatization. Participants learned to associate abstract images with right or left button presses explicitly before strengthening these associations through stimulus–response trials with (i.e., Session 1) and without (i.e., Session 2) feedback. In Session 1, trials were divided into response-selection and feedback events to separately assess decision versus learning processes. Session 3 evaluated stimulus–response automaticity using a location Stroop task. DS activity correlated with response-selection and not feedback events in Phase 1 (i.e., Blocks 1–3), Session 1. Longer response times (RTs), lower accuracy, and greater intertrial variability characterized Phase 1, suggesting deliberation. DS activity extinguished in Phase 2 (i.e., Blocks 4–12), Session 1, once RTs, response variability, and accuracy stabilized, though stimulus–response automatization continued. This was signaled by persisting improvements in RT and accuracy into Session 2. Distraction between Sessions 1 and 2 briefly reintroduced response uncertainty, and correspondingly, significant DS activity reappeared in Block 1 of Session 2 only. Once stimulus–response associations were again refamiliarized and deliberation unnecessary, DS activation disappeared for Blocks 2–8, Session 2. Interference from previously learned right or left button responses with incongruent location judgments in a location Stroop task provided evidence that automaticity of stimulus–-specific button-press responses had developed by the end of Session 2. These results suggest that DS mediates decision making and not late-stage learning, reconciling two, independently evolving and well-supported literatures that implicate DS in different cognitive functions. *Hum Brain Mapp 38:6133–6156, 2017.*

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INTRODUCTION

The dorsal striatum (DS)—the bulk of the caudate nucleus and putamen—has long been implicated in stimulus–response learning [Ashby et al., 2007; Yin and Knowlton, 2006]. The DS is ascribed a role in both early, goal-directed learning [Brovelli et al., 2011; O'Doherty et al., 2004] and late-stage learning of stimulus–response associations to the point of automaticity [Ashby et al., 2010; Balleine et al., 2009]. Challenging this notion, however, learning is often preserved in patients [Exner et al., 2002; Hiebert et al., 2014a; MacDonald et al., 2013b; Vo et al., 2014] and in animals [Atallah et al., 2007] with DS dysfunction. Features of standard stimulus–response learning methodology potentially shed light on this controversy as detailed in the paragraphs below.

Disentangling Learning and Decisions Guided by Learning

Decision-making and learning processes are confounded in standard stimulus–response learning methodologies [Jessup and O'Doherty, 2011; McDonald and Hong, 2004]. Trials typically proceed as follows: (a) a stimulus is presented and participants decide among a set of responses and (b) feedback regarding accuracy is provided, shaping stimulus–response associations. Learning is generally measured by the accuracy in selecting responses. Consequently, failing either to acquire stimulus–response associations or to select accurate responses based on these learned associations could lead to impaired performance in these paradigms. In this way, in standard paradigms, evaluation of learning and decision making is ambiguous. Further, in functional magnetic resonance imaging (fMRI) studies, (a) selecting a response and enacting it and (b) learning from feedback regarding the appropriateness of the response are typically treated as a single event with all significantly activated brain regions ascribed a role in learning *per se* [Dobryakova and Tricomi, 2013; Jessup and O'Doherty, 2011; Poldrack et al., 1999]. Accordingly, some brain regions that might underlie decision processes guided by learned associations could erroneously be assigned a role in learning. Given that these processes are temporally intertwined and functionally interdependent, distinguishing them is very challenging, requiring novel experimental designs, and nuanced interpretations. Learning and decision selection are entirely distinct processes phenomenologically, however. Distinguishing neural substrates of these different operations is important, with implications for understanding cognition in health and disease.

Recently, we investigated this issue in early, goal-directed learning using fMRI [Hiebert et al., 2014b]. Participants learned to associate abstract images with button presses through deterministic feedback. We modeled (a) the phase during which participants decided amongst options and selected responses separately from (b) the stage when participants learned about associations through feedback regarding the accuracy of their choices. We found activation of DS—specifically the head of the caudate nucleus—only during the decision enactment phase, not during the feedback phase when participants learned the associations based on outcome information. Furthermore, DS activation during the decision stage of our trials only occurred for trials arising later in the learning session, when the slope of learning was shallower but when participants were beginning to have a basis on which to make response selections, guided by associations that they had acquired in the earliest trials. In contrast, activity in the ventral striatum (VS)—consisting of the nucleus accumbens and most ventral parts of the caudate nucleus and putamen—correlated with the feedback phase of our stimulus–response learning trials as has been shown by others [Cools et al., 2007; Schultz et al., 1992]. Feedback-related VS activation was greatest in the earliest phase of learning when the slope of behavioral change, indicative of stimulus–response association learning, was steepest.

DS Mediates Late-Stage Learning and Automaticity?

The findings of Hiebert et al. [2014b] were (a) consistent with the view that DS mediates decisions regarding response selection and (b) inconsistent with the contention that DS mediates early, feedback-based learning, as has previously been prevalently claimed [Balleine et al., 2009; Boettiger and D'Esposito, 2005; Brovelli et al., 2011; Brown and Stern, 2013; Foerde et al., 2013; Garrison et al., 2013; Hart et al., 2013; O'Doherty et al., 2004]. However, a role for DS in other forms of learning that do not depend upon feedback or that occur during later stages of stimulus–response association formation could not be ruled out. Indeed, in addition to claims that the DS mediates early learning, the DS, particularly the body and tail of the caudate nucleus, has also been implicated in later stages of learning, when stimulus–response associations are strengthened through repeated experience to the point that they become automatic [Ashby et al., 2007; Helie et al., 2010].

A prominent theory of automaticity suggests that the role of the DS—*specifically the body and tail of the caudate*

nucleus—is to acquire associations and train cortical–cortical connections between higher order sensory and premotor areas [Ashby et al., 2007; Helie et al., 2010]. This model of automaticity is referred to as Subcortical Pathways Enable Expertise Development (i.e., SPEED; Ashby et al. [2007]). SPEED predicts that subcortical regions mediate learning. The theory maintains that the head of the caudate nucleus mediates early learning, and as the associations become more practiced, progressing toward automaticity, more posterior regions of the striatum, namely the body and tail of the caudate nucleus, underlie late-stage learning. Once automaticity has been achieved, involvement of DS ceases, and stimulus-specific, automatic behaviors become mediated by cortical regions (i.e., premotor, motor, and visual cortices; Ashby et al. [2007]).

Balleine and O'Doherty [2010], however, go further contending that in addition to being implicated in training stimulus–response habits, DS mediates and sustains habitual or automatic responding even once these associations are well entrenched [Balleine and O'Doherty, 2010; Everitt and Robbins, 2005; Tricomi et al., 2009]. Though several human studies of habit learning ascribe habit formation to DS (i.e., dorsal putamen), closer examination reveals that the ventral, posterior putamen (e.g., peak coordinates $z = 0$) is often the region preferentially activated during these pivotal learning studies [Balleine and O'Doherty, 2010; Tricomi et al., 2009; but see Wunderlich et al., 2012, implicating dorsal putamen]. It is widely accepted that VS and DS are functionally distinct [Atallah et al., 2007; MacDonald and Monchi, 2011; van der Meer and Redish, 2011]. Indeed, others explicitly claim that posterior ventral putamen (i.e., VS) mediates overlearning of motor responses [Jueptner et al., 1997; Lehericy et al., 2005].

In a study implicating DS in the development of automatic behaviors, Helie et al. [2010] investigated automatization of responses in a category learning paradigm that included over 10,000 trials, across 20 separate learning sessions, with fMRI data obtained in Sessions 1, 4, 10, and 20. They found that activity in DS was increased throughout Session 1, at the end of which high levels of response accuracy were ultimately achieved (i.e., 89.6%). In subsequent sessions, DS activity was significantly attenuated (i.e., after Session 1), whereas cortical activation continued to correlate with accurate categorization even after extensive training. Only neural activity correlating with stimulus–response events (i.e., the time period from the onset of the stimulus to the button-press response) was examined. Given the confounding of decision and learning processes in these methodologies and consistent with our claim in Hiebert et al., [2014b], DS activation at the time of response selection and enactment could have arisen due to its involvement in decision-making processes and not with association learning *per se*. Several other studies cited as support for the SPEED model can be reinterpreted similarly to the findings of Helie et al. [2010], concluding that DS activation arises not due to its role in learning but rather due to its role in decision-making processes [Poldrack et al., 2005; Wu et al., 2004]. As with studies of early stimulus–response learning, most experiments investigating DS's role in late-stage learning combine and confound learning processes and stimulus-specific response-selection processes [O'Doherty et al., 2004; Tricomi et al., 2009].

DS Mediates Decision Making?

Indeed, a reinterpretation of these early- and late-learning experiments, considering the facts that decision making and stimulus–response association learning (a) depend upon one another to produce accurate performance and (b) are often merged in fMRI studies, could integrate two divergent and extensive literatures regarding DS's role in cognition. Increasingly, DS is linked to response selection and decision making [Atallah et al., 2007; Grahn et al., 2009; Jessup and O'Doherty, 2011; MacDonald et al., 2014a]. Decision making is defined as the process of representing and assigning values to different response possibilities, then selecting and executing the most appropriate action [Rangel et al., 2008]. DS has particularly been ascribed a role in decision making when decisions require a degree of reflection, when there is some ambiguity, and when cognitive control or flexibility are required. This process is referred to as *deliberation* [Ali et al., 2010; Cools and D'Esposito, 2011; Daniel et al., 2010; DeGutis and D'Esposito, 2007; MacDonald et al., 2011; Ohira et al., 2010; Robertson et al., 2015]. In this way, DS is implicated prominently in this literature in *resisting* habitual responding or attending to more salient stimuli [Balleine et al., 2009; Benke et al., 2003; Cameron et al., 2010; Cools, 2006; Cools et al., 2009; Hiebert et al., 2014b; MacDonald et al., 2011; Rieger et al., 2003; Robertson et al., 2015], completely at odds with the independently evolving literature linking DS with stimulus–response learning and automatization.

In categorization tasks, DS activity, assessed with neuroimaging, correlates with decision accuracy when options need to be weighed but not once responses become so well-practiced that reflection is unnecessary [Helie et al., 2010; Soto et al., 2013]. Preferential DS activation is observed for ambiguous relative to unambiguous decisions [DeGutis and D'Esposito, 2007; MacDonald et al., 2011; Schouppe et al., 2014], supporting a role for DS in the process of deliberation. Further, patients with DS dysfunction are *less* impaired than healthy control participants at attending to more salient stimuli among distractors and choosing more practiced responses among competing alternatives [Cameron et al., 2010; Cools et al., 2009; Hood et al., 2007], but they are *more* impaired when they are required to select less salient stimuli or perform less automatic responses relative to alternatives [Benke et al., 2003; Cameron et al., 2010; Cools et al., 2006, 2009; Hood et al., 2007; Rieger et al., 2003; Thoma et al., 2008], suggesting that DS's role in decision making is to promote deliberation and prevent poorly considered or

impulsive choices. These claims are at odds with prevalent theories ascribing a role for DS in automatization of responses and selection of habitual actions [Everitt and Robbins, 2005] and therefore requires direct investigation to reconcile these contradictory contentions regarding DS's role in cognition.

This Study

Here, we critically tested the claim that DS mediates automatization of stimulus-specific responses versus the notion that it underlies deliberation during action selection. We investigated later-stage, stimulus–response learning, once performance accuracy was greater than 90%. We estimated striatal brain activity using fMRI along with behavior during later-stage, stimulus–response learning. We further included an explicit measure of whether stimulus–response associations achieved automaticity. We closely paralleled Hiebert et al. [2014b], but used fewer stimuli and only two responses, right or left button presses. Further, we began with an explicit learning phase—a shortcut to late-stage learning—during which all stimuli in the experiment were presented and assigned to either the right or left button press. Subsequently, as in Hiebert et al. [2014b], stimulus–response learning took place in an implicit, feedback-based manner (Session 1), followed by further implicit strengthening of these associations through repeated stimulus–response trials with feedback removed (Session 2). We investigated neural activity for decision-making and feedback events separately in Session 1 and for decision-making events only in Session 2. Between Sessions 1 and 2, we implemented a 20-min distractor task with the aim of (1) testing whether stimulus–response automaticity was achieved by the end of Session 1 and (2) reintroducing an element of uncertainty and deliberation for decisions in Block 1 of Session 2. The appearance of preferential blood-oxygenation-dependent (BOLD) signal in DS immediately following distraction therefore could critically distinguish between notions that DS mediates the development of stimulus–response association automaticity versus decisions requiring reflection. Finally, Session 3 consisted of a location Stroop task as a second, objective test of whether stimulus-specific responses were automatized following Sessions 1 and 2. In this final session, participants indicated the location, with right or left button presses, of stimuli that had previously been paired with right or left button-press responses during learning Sessions 1 and 2 versus novel stimuli.

We also performed a second, supplemental experiment using a similar protocol to the one summarized in the preceding paragraph, to further clarify our findings (see Experiment 2 in Supporting Information). Experiment 2 differed from the Main Experiment in the following ways: (1) neural activity was not estimated with fMRI and (2) an additional session of the modified location Stroop task was also included immediately after Block 3 (i.e., Phase 1, explained below) in Session 1.

Predictions

If DS underlies the development of automaticity as suggested by SPEED, BOLD signal in DS should persist for stimulus-specific responses until associations achieve automatic status (i.e., throughout Session 1, and possibly in Session 2 depending on explicit measures of automaticity). We included two measures of stimulus–response automaticity. At the end of Session 1, we examined the effect of an intervening task on stimulus–response performance and BOLD signal. If automaticity had developed prior to the end of Session 1, response time (RT), accuracy, and BOLD signal should be unchanged from Phase 2, Session 1, and Session 2 despite an intervening distraction (see Ashby et al. [2010] for a review). At the end of Session 2, we investigated facilitation and interference in a location Stroop task, related to automaticity of previously-learned, stimulus-specific right and left button presses. If automaticity had developed by the conclusion of Sessions 1 and/or 2, (a) faster RTs and/or reduced errors should occur when location button presses matched the button press that had previously been associated with the stimulus in Sessions 1 and 2, and/or (b) slower RTs and/or increased errors should occur when location button presses mismatched the button press that had previously been associated with the stimulus in Sessions 1 and 2.

In contrast, if DS mediates deliberation in response selection, DS activity should be maximal in very early phases of the Main Experiment when decision making requires greater consideration, indexed by longer RTs, lower accuracy, and greater response variability (Phase 1, Session 1). Response variability was measured by changes in standard deviation of RTs (SD). Activity in DS should attenuate and disappear, even prior to achievement of automatic responding, once responses become sufficiently well-learned that deliberation is unnecessary (Phase 2, and Session 2), signaled by reduced RT, accuracy, and/or response variability. To further distinguish these views, following an unrelated, intervening task, DS BOLD signal is expected to (a) reappear in the first block when response deliberation would again be required (i.e., Block 1, Session 2) but (b) quickly attenuate due to savings when responses again became well-practiced (Blocks 2–8, Session 2).

Disputing the claim that DS underlies late-stage learning to the point of stimulus–response automaticity using fMRI can only be accomplished by showing that DS BOLD signal is dissociated from this process, attenuating *before* automaticity of stimulus–response associations is actually achieved. In this way, this well-entrenched view about DS's role in behavior can only be contested by accepting a null result. There is a, perhaps, justified bias against publishing negative findings, in that with frequentist approaches, the probabilities of Type II (i.e., falsely failing

to reject the null hypothesis) and Type I errors (i.e., falsely rejecting the null hypothesis) are asymmetric. Type I errors are set a clear maximum, usually less than 0.05, whereas the former varies across studies in terms of its magnitude and determinants [Dienes, 2014] not predetermined by the experimenter. However, this systematic publication bias contributes to extremely slow changes to the status quo with the effect that once a claim is disseminated and relatively accepted, it becomes nearly irrefutable, a process referred to as *canonization* [Nissen et al., 2016]. Findings at odds with prevailing views are considered less publication-worthy and held to a far higher standard [Nissen et al., 2016]. Computational models, however, reveal that selective publication and omission of negative results does not improve efficiency or accuracy of scientific inquiry, but does increase false canonization [Nissen et al., 2016; van Assen et al., 2014]. These concerns notwithstanding, to critically test the contention that DS underlies late learning versus deliberation in action selection and to increase confidence in our results, we have introduced a number of manipulations (e.g., distraction separating Sessions 1 and 2) that should predictably alter behavior and DS BOLD signal in distinct ways to dissociate the differing accounts of DS's role in cognition. Furthermore, in addition to frequentist statistical approaches, we planned to investigate our effects using a Bayesian analysis that allows directly contrasting the probability of the null and the alternative hypotheses in a symmetrical way, putting these hypotheses on an equal footing, and directly comparing the relative fit of the two models [Dienes, 2014]. This approach would allow us greater confidence in our interpretation of null results if they arose, as we predicted.

MATERIALS AND METHODS

Participants

Nineteen healthy, young, right-handed adults participated in this experiment (10 males and 9 females). Participants had a mean (standard error measure; SEM) age and duration of education of 23.56 (0.83) and 16.63 (0.46) years, respectively. One participant was excluded from analysis due to excessive head motion while in the scanner, whereas another was excluded for falling asleep in the scanner. Two participants were subsequently excluded from Session 3 only, due to a misinterpretation of the task instructions. Participants abusing prescription or illicit drugs, alcohol, or taking cognitive-enhancing medications including methylphenidate were excluded from participating in the experiment. The Health Sciences Research Ethics Board of the University of Western Ontario approved this study. All participants provided informed, written consent to the approved protocol before beginning the experiment, according to the Declaration of Helsinki (2013).

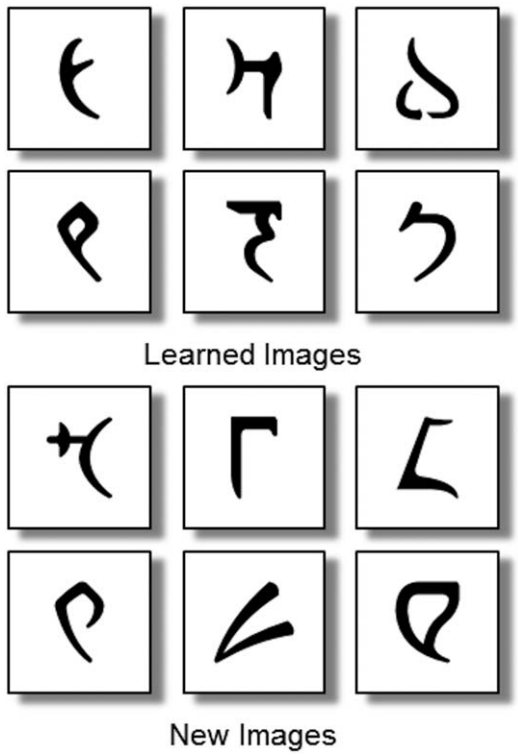

Figure 1.

Abstract images presented in the experiment. Learned images refer to the images that were studied and associated with a specific "right" or "left" button-press response at baseline, via deterministic feedback in Sessions 1 and 2. In Session 3 (3A and B in Experiment 2), these learned images created the conditions for the congruent and incongruent conditions depending on their location of presentation. New images refer to the images presented only in Session 3 (i.e., 3A in the Main Experiment and 3A and 3B in Experiment 2) that constituted the control condition.

Procedures

At the outset, all participants explicitly learned to associate six abstract images with one of two button-press responses prior to fMRI Sessions 1, 2, and 3. Images consisted of characters taken from the invented *Klingon* alphabet (Fig. 1). The six abstract images appeared on the screen. Three were labeled "left button press" and the other three were labeled "right button press". Participants were given 3 min to memorize the label given to the images as best they could.

Figure 2 depicts the experimental protocol of the Main Experiment. In Session 1, on every trial, one of the six stimuli presented in the baseline learning session appeared in the center of the projection screen. Participants were asked to perform the button-press response that had been assigned to the stimulus. For stimuli assigned to a left button press, participants were instructed to press the left

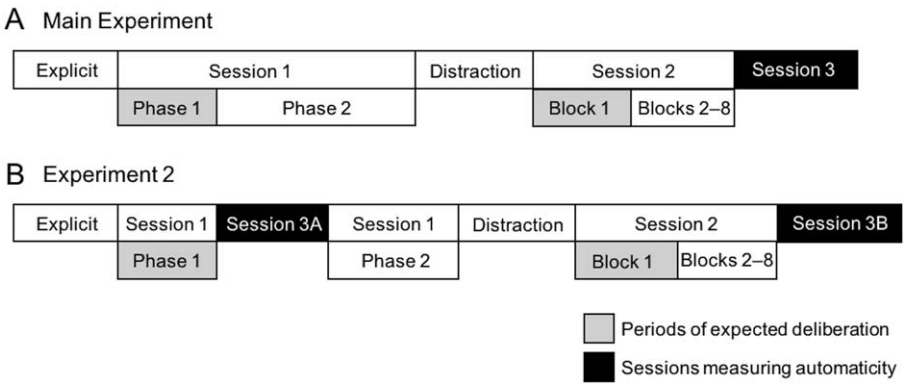

Figure 2.

Experimental protocol. (**A**) In the main experiment, participants learned to associate six abstract images with either a "left" or "right" button press response explicitly in the block named Explicit. In Session 1, participants saw each image and performed the learned response individually in the presence of feedback. Due to longer RTs, lower accuracy, and increased response variability, the first three blocks (referred to as Phase 1) were analyzed separately from Blocks 4 to 12 (i.e., Phase 2). After completing a distractor task for 20 min, participants performed Session 2 where they practiced the learned responses to the images in the absence of feedback. We expected response uncertainty to reappear in Block 1, Session 2 and we therefore analyzed it separately from Blocks 2 to 8, Session 2. Session 3 served as an objective measure of automaticity and was performed after Session 2 concluded. (**B**) Experiment 2 followed the same protocol as the Main Experiment except that the presence of automaticity was measured both after Phase 1, Session 1 and after Session 2 (Session 3A and 3B, respectively). Areas in grey represent periods where response deliberation is expected and areas in black denote the modified Stroop task (i.e., objective measure of automaticity).

button on the button box with their index finger. For stimuli assigned to the right button press, participants were asked to press the right button on the button box with their middle finger. All responses were performed with the right hand. Deterministic feedback regarding the accuracy of the response was then provided (i.e., "Correct" or "Incorrect") during a feedback event. Trials were organized into four scanning runs, with each run consisting of three blocks of 18 trials, for a total of twelve blocks and 216 trials, each abstract image occurring three times in random order per block. At the end of the 12th block, participants were given a score summarizing their overall performance. Trials in Session 1 proceeded as follows: (i) a cross appeared in the center of the projection screen for 700 ms; (ii) a blank screen occurred for 300 ms; (iii) an abstract image was presented in the center of the projection screen until a button-press response; (iv) a blank screen appeared for a variable period of time sampled from an exponential distribution (mean: 2500 ms; minimum: 525 ms; maximum: 7,000 ms); (v) feedback (i.e., "Correct" or "Incorrect") appeared for 1,000 ms; (vi) a blank screen appeared for a variable period of time sampled from an exponential distribution (mean: 2500 ms; minimum: 525 ms; maximum: 7,000 ms). The interstimulus interval (ISI) and intertrial interval (ITI) were jittered between the response and feedback, and between the offset of feedback and the beginning of the subsequent trial, respectively, to create two fMRI events within each trial: (a) the stimulus–response event and (b) the feedback event. The stimulus–response or decision-making event included the presentation of the abstract image until the participant made a button-press response. The feedback or learning event included the presentation of feedback. Rest events were also created and modeled as regressors and consisted of ITIs only (Fig. 3A).

Between Sessions 1 and 2, participants performed a 20-min visual-spatial working memory task as a distraction from the main task. The task consisted of prime and probe pairs in which participants indicated, with a button press, whether an array of dots inside a grid pattern was the same or different across the prime and probe trials. The distractor task was included to reintroduce an element of uncertainty and deliberation in selecting responses in the first block of Session 2.

In Session 2, on every trial, participants performed a right or left button press in response to the image that appeared in the center of the screen. The images were the same six Klingon characters presented at the start of the experiment and in Session 1. Participants were asked to make the button-press responses that they had learned explicitly at the outset of the experiment and through Session 1 in Session 2. No feedback was provided, to preclude further feedback-based learning during Session 2. Participants performed eight blocks of 18 trials each, spaced across two scanning runs, four blocks per run. In total, Session 2 consisted of 144 trials. Trial parameters for Session 2 were otherwise identical to those in Session 1 (Fig. 3B).

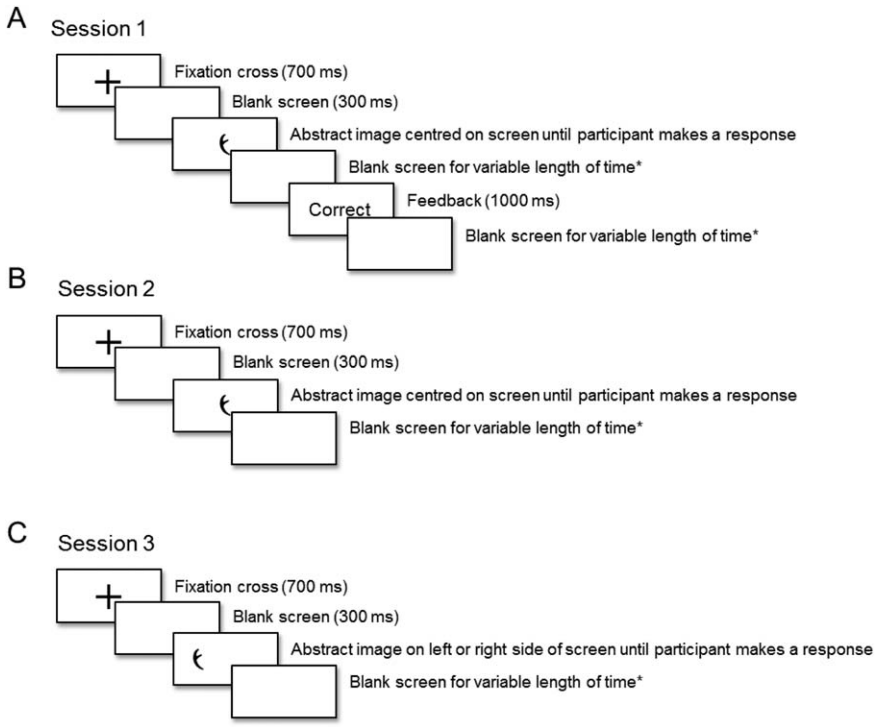

Figure 3.

Example of a single trial in Sessions 1, 2, and 3 in the experiment. (**A**) Participants learned to associate six abstract images with either a "left" or "right" button-press response in Session 1. The following is an example of a trial: (i) a cross appeared in the center of the projection screen for 700 ms; (ii) a blank screen occurred for 300 ms; (iii) an abstract image was presented in the center of the projection screen until a button-press response; (iv) a blank screen appeared for a variable period of time sampled from an exponential distribution (mean: 2,500 ms; minimum: 525 ms; maximum: 7,000 ms); (v) feedback (i.e., "Correct" or "Incorrect") appeared for 1,000 ms; (vi) a blank screen appeared for a variable period of time sampled from an exponential distribution (mean: 2,500 ms; minimum: 525 ms; maximum: 7,000 ms). (**B**) Participants recalled the responses to the learned images in the absence of feedback in Session 2. (**C**) Images appeared left or right of center, at a distance equal to the width of the image away from center, and participants indicated the location of the images with a left or right button-press response. Stimuli included the six learned images presented at baseline and in Sessions 1 and 2 and six new images. Trials in Sessions 2 and 3 were identical to Session 1 except that feedback was omitted in both and the images appeared off center in Session 3. *The interstimulus and intertrial intervals (ISI and ITI, respectively) were jittered between the response and feedback and between the offset of feedback and the beginning of the subsequent trial to create two fMRI events within each trial: (a) the stimulus-response event and (b) the feedback event for Session 1. In Sessions 2 and 3, the ITIs were jittered between the response and the subsequent trial.

In Session 3, the six images associated with left or right button-press responses explicitly at the outset of the experiment and throughout Sessions 1 and 2 were presented along with six new *Klingon* characters. Images were presented one at a time, in random order. These images were presented either to the left or the right of center, with a distance away from the center equal to the width of the image. Participants responded to the location of the stimulus with the left (i.e., index finger) or right (i.e., middle finger) button-press response. No feedback was provided in this session. Participants performed 4 blocks of 36 trials each, spaced across two scanning runs, two blocks per run. In total, Session 3 consisted of 144 trials and no feedback was provided. Trial parameters were similar to Sessions 1 and 2 (Fig. 3C).

Behavioral Data Analysis

To examine changes in RT, SD of RTs across blocks, and accuracy across Sessions 1 and 2, single-factor repeated measures analyses of variance (ANOVAs) were run with block (Session 1: 12 blocks; Session 2: 8 blocks) as the within-subject variable. RT was the time between the onset of the abstract image and the button press by the participant measured in milliseconds (ms). The number of

correct "right" and "left" button-press responses recorded after each block was our estimate of accuracy.

Three conditions—congruent, incongruent, and control—were created in Session 3. In the congruent condition, an image appeared in a location that was consistent with the left or right button-press response learned for that image at baseline and in Session 1, and practiced in Session 2. In the incongruent condition, a stimulus appeared in a location that was inconsistent with the left or right button-press response learned at baseline and in Session 1, and practiced in Session 2. In the control condition, six new images that were not previously presented in the experiment appeared to the left or right of center. Session 3 consisted of 48 congruent, 48 incongruent, and 48 control trials that occurred in random order. All old and new stimuli appeared left and right of center equally often. RTs were measured from the onset of the image until the button-press response in milliseconds. The control condition provided a baseline measure of accuracy and latency for providing a location response. Facilitation was calculated as mean RTs or error rates in the congruent condition minus those in the control condition and interference was calculated as mean RTs or error rates in the incongruent condition minus those in the control condition. Last, congruent and incongruent trials together were contrasted with control trials to assess trials that involved previously learned stimuli that could distract from choosing location responses versus the condition in which there were no previously learned stimulus-identity responses to distract from location responses.

One-sample *t* tests were run on the facilitation and interference scores to assess if they were significantly different from zero. These analyses provided an objective test of whether the stimulus–response associations had been learned to the point that the responses were automatic.

Imaging Acquisition

FMRI data were collected on a 3 T Siemens Magnetom Prisma with Total Imaging Matrix MRI at Robarts Research Institute at the University of Western Ontario. A scout image for positioning the participant and a T1 for anatomical localization were first obtained. Session 1 consisted of four runs of T2*-weighted functional acquisitions. Each run consisted of three blocks of 18 trials. A distractor task (20 min) was administered after Session 1. Session 2 consisted of two experimental runs. Each run comprised four blocks of 18 trials. Session 3 was completed as the final session and consisted of two experimental runs, with each run containing 2 blocks of 36 trials. In each of the experimental sessions, the repetition time was 2.5 s with one whole-brain image consisting of 43 2.5-mm-thick slices. The field of view was oriented along the anterior and posterior commissure with a matrix of 88 × 88 pixels, with an isotropic voxel size of 2.5 × 2.5 × 2.5 mm^3. The echo time was 30 ms and the flip angle was 90°.

FMRI Data Analysis

Matrix Laboratory (MATLAB, MathWorks, Inc., Natick, Massachusetts, United States) was used in conjunction with Statistical Parametric Mapping version 8 (SPM8; Wellcome Department of Imaging Neuroscience, London, United Kingdom) to complete fMRI analysis. Images were slice-time corrected, reoriented for participant motion, spatially normalized to the standard Montreal Neurological Institute (MNI) template, smoothed with an 8 mm full-width half-maximum Gaussian kernel, and high-pass filtered (0.0078 Hz).

Fixed-effects analyses were used to model individual participant's data in SPM8. Regressors were created by convolving onsets and durations of stimulus–response, feedback, and rest (i.e., the ITI) events with the canonical hemodynamic response function. The stimulus–response event was defined as the time from onset of the *Klingon* character until the participant made a button-press response. The feedback event was defined as the duration of feedback (i.e., "Correct" or "Incorrect") presentation (i.e., 1,000 ms from onset to offset). The rest period modeled was the time between the offset of the feedback until the fixation point of the subsequent trial (i.e., the ITI). A general linear model (GLM) was created for Session 1 events and included regressors for stimulus–response, feedback, and rest events for Session 1 and investigated regional BOLD activity associated with these events. There were 12 regressors for each of the three events, corresponding to each of the 12 blocks in Session 1. Six rigid-body realignment parameters were entered as nuisance regressors to minimize the effect of head motion. A similar model was created for stimulus–response and rest events for Session 2. There were a total of 16 regressors, two per block, eight of which corresponded to stimulus–response events and the other eight for rest events. Motion regressors were also included in the Session 2 GLM.

To investigate learning versus deliberation-related brain activity, contrasts at the group level were created, examining activity early and late in Session 1 for both stimulus–response and feedback events. Given the significant decreases in RT, SD of RTs, and significant increases in accuracy in Session 1 across the first three blocks, that subsequently levelled off (Fig. 4A), Blocks 1–3 were assigned early status, referred to as Phase 1, and Blocks 4–12 were considered late, referred to as Phase 2. Similarly, for Session 2, we investigated Block 1 and Blocks 2–8 separately, with the expectation that a 20-min distractor task might reintroduce an element of consideration in stimulus–response selection but only for the earliest block due to savings and substantial previous experience with the stimulus–response pairs.

For Session 3, regressors were created convolving onsets and durations of congruent, incongruent, and control trials. At the group level, activation correlating with facilitation and interference was investigated by contrasting

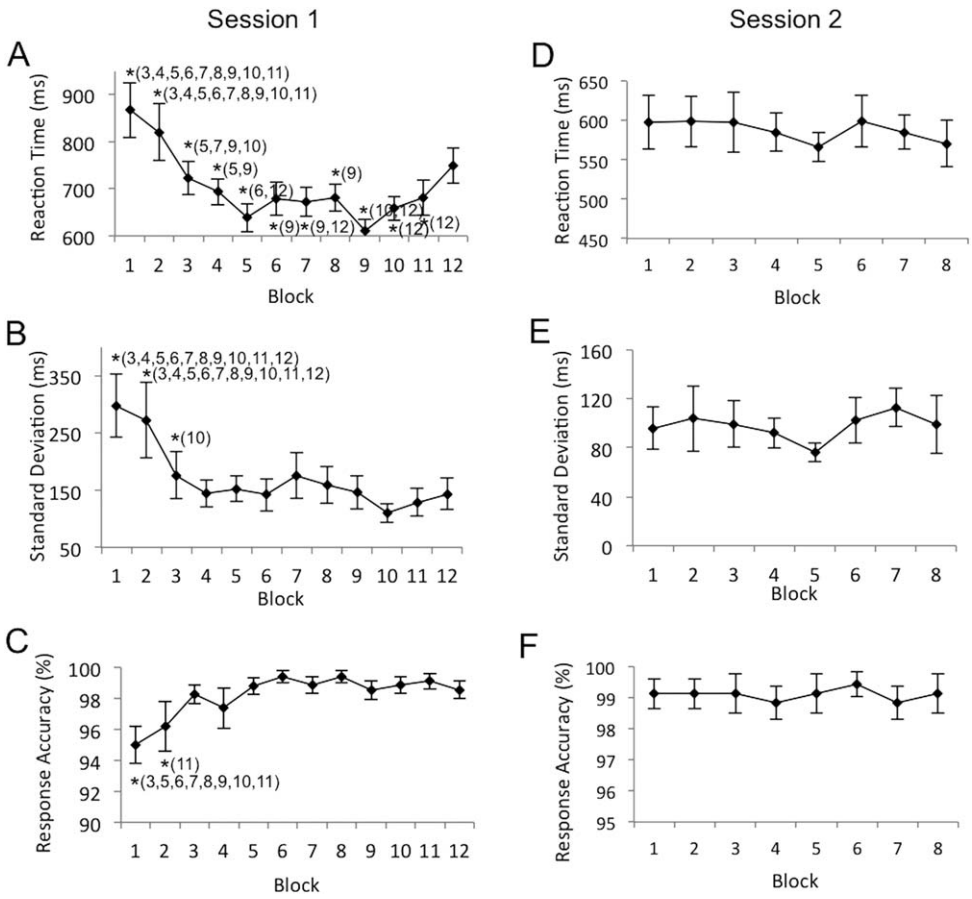

Figure 4.

Mean response times, standard deviations, and accuracy across Sessions 1 and 2. (**A**) Mean response times (ms) in each block in Session 1. (**B**) Mean standard deviations (ms) calculated using response times in each block in Session 1. (**C**) Mean response accuracy (%) in each block in Session 1. (**D**) Mean response time (ms) in each block in Session 2. (**E**) Mean standard deviations (ms) calculated using response times in each block in Session 2. (**F**) Mean response accuracy (%) in each block in Session 2. Error bars represent standard error of the mean. Response time was measured from the onset of the abstract image to the button-press response made by the participant. Response accuracy is a percentage measure of the number of correct button-press responses in a block relative to total number of trials in the block. Significant differences ($P < 0.05$) are indicated with an asterisk (*) and numbers listed next to the asterisk indicate the blocks from which each block differs significantly.

activation of congruent with control trials for facilitation and incongruent with control trials for interference.

Peaks within the striatum were reported at a significance level of $q < 0.05$ cluster-corrected using false discovery rate (FDR) correction unless otherwise indicated. Striatal regions were defined using the Harvard-Oxford Subcortical Atlas in the FMRIB Software Library version 5.0 (FSL v5.0; Analysis Group, FMRIB, Oxford, United Kingdom). VS and DS are not distinct anatomical structures, which creates difficulty when attempting to separate them in an fMRI context. In a review, Postuma and Dagher [2006] define VS as $z \leq 2$, which we employed. Here, DS refers to portions of the caudate nucleus and putamen at a level *of* $z > 2$ in MNI space. VS was defined as the nucleus accumbens, and the caudate nucleus and putamen at a level *of* $z \leq 2$ in MNI space. All cortical regions were defined using the Harvard-Oxford Cortical Atlas in the FMRIB Software Library version 5.0 (FSL v5.0; Analysis Group, FMRIB, Oxford, United Kingdom). All x, y, and z coordinates are reported in MNI space.

The contrasts of interest for Sessions 1, 2, and 3 were as follows: (i) stimulus–response events versus rest in Phase 1 of Session 1; (ii) feedback events versus rest in Phase 1 of Session 1; (iii) stimulus–response versus feedback events in Phase 1 of Session 1; (iv) stimulus–response events versus rest in Phase 2 of Session 1; (v) feedback events versus rest in Phase 2 of Session 1; (vi) stimulus response versus feedback events in Phase 2 of Session 1; (vii)

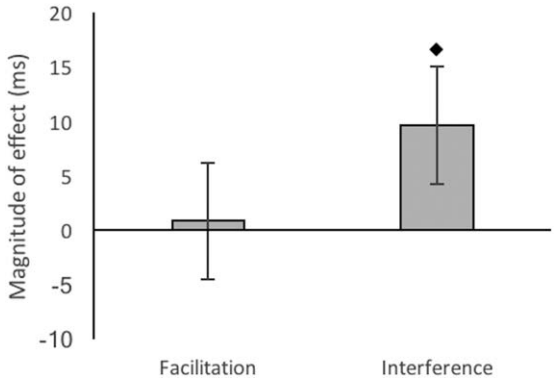

Figure 5.

Mean Facilitation and Interference scores in Session 3. Mean (SEM) facilitation, interference, and incongruent minus congruent difference scores are presented. Facilitation was calculated as mean RTs in the congruent minus control condition and interference was calculated as mean RTs in the incongruent minus control condition. The incongruent minus congruent contrast was also completed. Again, in the congruent condition stimuli were presented in the location that was consistent with the learned left or right button-press responses in earlier sessions. On incongruent trials, stimuli were presented in the location that was inconsistent with the learned left or right button-press responses in earlier sessions. The control condition consisted of new images that the participant had not previously associated with a right or left button-press response. $*P < 0.05$, $\omega P < 0.1$

stimulus–response events of Phase 1 versus stimulus–response events of Blocks 4, 5, and 6, Blocks 7, 8, and 9, and Blocks 10, 11, and 12 of Session 1; (viii) stimulus–response events in Block 1 of Session 2 versus rest; (ix) stimulus–response events for Blocks 2–8 versus rest; (x) stimulus–response events for Block 1 versus Block 8 of Session 2; (xi) facilitation in Session 3; (xii) interference in Session 3; and (xiii) congruent and incongruent versus control trials in Session 3. Phase 1 refers to Blocks 1–3 in Session 1 and Phase 2 refers to Blocks 4–12 in Session 1, based on behavioral data patterns presented below.

Bayesian Analysis

Bayesian analyses were performed. Bayes' factor one-sample *t*-tests were conducted using the average beta values extracted in each block of Sessions 1 and 2, and for all contrasts of conditions (i.e., congruent, incongruent and control) in Session 3, using a bilateral dorsal caudate nucleus ROI. The dorsal caudate nucleus anatomical ROI was created using the Automated anatomical labeling atlas [Tzourio-Mazoyer et al., 2002], and WFU PickAtlas [Maldjian et al., 2003] in conjunction with MarsBaR [Brett et al., 2002]. The ROI included left and right dorsal caudate nucleus at a level of $z > 2$ mm in MNI space. With a test value of zero, the Bayesian analysis examined whether the extracted beta values were significantly greater than zero using the Bayes' factor of three, previously indicated to be the Bayesian corollary of $P < 0.05$ in frequentist hypothesis testing [Dienes, 2014]. If the Bayes' factor of the average beta values is <3, it strongly supports the null hypothesis that the activation level is not greater than zero.

RESULTS

Behavioral Data

RT was measured as the time between the onset of the abstract image and a button-press response by the participant in milliseconds. The number of correct "left" and "right" button-press responses recorded after each block provided our measure of accuracy. Behavioral results are presented in Figures 4 and 5 and Tables I and II.

Session 1

The mean block RT, SD of RTs across blocks, and accuracy across Session 1 are shown in Figure 4A–C respectively. Mauchly's test was significant, indicating the assumption of sphericity was violated ($P < 0.001$). Therefore, degrees of freedom were corrected using the Greenhouse-Geisser Epsilon for the RT, SD of RTs across blocks, and accuracy single-factor repeated measures ANOVAs.

RTs were examined and revealed a main effect of block, $F_{(3,95)} = 9.34$, MSE = 63567.54, $P < 0.001$. Deconstructing this effect using pairwise comparisons revealed significant RT differences between Blocks 1 and 11 versus other subsequent blocks (see Table I and Fig. 4A for specific significant comparisons). No differences arose between Block 12 and other blocks. Mean RTs decreased from 867 ms in Block 1 to 749 ms in Block 12.

SD of RTs across blocks, within Participants, were investigated, and revealed a main effect of block $F_{(3,62)} = 5.07$, MSE = 11919, $P < 0.001$. Significant SD differences between blocks were examined using pairwise comparisons and revealed significant differences between Blocks 1 and 3 versus other subsequent blocks (see Table I and Fig. 4B for specific significant comparisons). No significant differences arose between Blocks 4–12 and other subsequent blocks. Mean SD decreased from 298 ms in Block 1 to 143 ms in Block 12.

The single-factor repeated measures ANOVA for accuracy revealed a significant main effect of Block, $F_{(4, 68)} = 3.03$, MSE = 33.07, $P = 0.025$. This was explored further using pairwise comparisons (results presented in Table I and Fig. 4C). Significant differences existed between Blocks 1 and 2 versus other subsequent blocks in Session 1. No significant differences arose between blocks later than 2 with one another. The average Block 1 score was 95.01%, which increased to 98.54% in Block 12.

Session 2

Mean RT in Block 1, Session 2 was significantly faster than the last block of Session 1 ($t = 1.86$, $P = 0.044$).

TABLE I. Significant pairwise comparisons for RT, SD, and accuracy differences by block in Session 1 of Experiment 1

		RT		SD		Accuracy	
Block A	Block B	*t* stat	*P* value	*t* stat	*P* value	*t* stat	*P* value
1	3	3.73	0.002	3.43	0.005	3.06	0.008
	4	4.07	<0.001	4.32	0.001	-	-
	5	4.07	<0.001	4.09	0.002	3.39	0.004
	6	4.07	<0.001	4.39	0.001	3.39	0.004
	7	4.07	<0.001	3.45	0.005	3.39	0.004
	8	4.07	0.001	3.90	0.002	3.39	0.004
	9	4.07	<0.001	4.26	0.001	2.75	0.015
	10	4.07	<0.001	5.28	<0.001	3.20	0.006
	11	3.39	0.004	4.76	<0.001	>4.07	<0.001
	12	-	-	4.35	0.001	2.95	0.010
2	3	2.75	0.015	2.70	0.020	-	-
	4	3.54	0.003	3.59	0.004	-	-
	5	>4.07	<0.001	3.36	0.006	-	-
	6	4.07	0.001	3.67	0.003	-	-
	7	4.07	0.001	2.73	0.020	-	-
	8	3.12	0.007	3.17	0.009	-	-
	9	>4.07	<0.001	3.53	0.004	-	-
	10	4.07	0.001	4.56	<0.001	-	-
	11	2.71	0.016	4.03	0.002	-	-
	12	4.07	0.001	3.62	0.004	-	-
3	5	2.82	0.013	-	-	-	-
	7	>4.07	<0.001	-	-	-	-
	9	3.06	0.008	-	-	-	-
	10	3.06	0.008	-	-	-	-
4	5	>4.07	<0.001	-	-	-	-
	9	2.28	0.038	-	-	-	-
5	6	2.75	0.015	-	-	-	-
	12	3.54	0.003	-	-	-	-
6	9	3.54	0.003	-	-	-	-
7	9	2.25	0.040	-	-	-	-
8	9	3.73	0.002	-	-	-	-
9	10	2.66	0.018	-	-	-	-
	12	3.73	0.002	-	-	-	-
10	12	3.54	0.003	-	-	-	-
11	12	3.00	0.009	-	-	-	-

Only significant ($P < 0.05$) comparisons are reported. The left column labeled Block A lists the blocks that differed significantly from blocks listed in column Block B. RT, response time; SD, standard deviation.

Accuracy in Block 1, Session 2 was not significantly different from accuracy in the last block of Session 1 ($t = 0.18$, $P = 0.429$). Mean block RT, SD of RTs across blocks, and accuracy across Session 2 are presented in Figure 4D–F, respectively. As in Session 1, single-factor repeated measures ANOVAs were run to investigate differences across Session 2. There were no significant differences across blocks for RT ($F < 1$), SD ($F < 1$), or response accuracy ($F < 1$) across Session 2.

Session 3

Data from two participants were excluded from analysis in Session 3 due to reported misinterpretation of the instructions of the task. The error rate in the remaining 17 participants was low (average incorrect responses: 0.74%). Table II presents the mean RTs and error rates in each of the congruent, incongruent, and control conditions. Paired *t* tests were performed on error rates between congruent and control, and incongruent and control. One-sample *t* tests were performed on average RT facilitation (i.e., congruent − control), and interference (i.e., incongruent − control; Fig. 6). There were significantly more errors in incongruent compared to control ($t = 2.06$, $P = 0.029$) conditions. In addition, RT interference compared to zero trended toward significance ($t = 1.37$, $P = 0.095$). However, facilitation ($t = -1.23$, $P = 0.881$) scores did not differ significantly from zero (Fig. 5).

FMRI Data

Significant activations are reported at a significance level of $q < 0.05$ FDR corrected unless otherwise stated using

TABLE II. Mean response times and error rates for the congruent, incongruent, and control condition in Session 3 of Experiment 1

Condition	Response time (ms)	Error rate (%)
Congruent	378.66 (17.44)	0.73 (0.17)
Incongruent	387.45 (20.66)	1.34 (0.39)
Control	377.84 (18.17)	0.98 (0.50)

Mean (SEM) response times (ms) and error rates (%) are presented. In the congruent condition, an image appeared in a location that was consistent with the left or right button-press response learned at baseline, in Session 1, and practiced in Session 2. In the incongruent condition, a stimulus appeared in a location that was inconsistent with the left or right button-press response learned at baseline, in Session 1, and practiced in Session 2. In the control condition, six new images that were not previously presented in the experiment appeared to the left or right of center.

SPM5 (Tables III–V). In all sessions, error rates were low and therefore only correct responses were examined at the group level. Session 1 contrasts are reported in Table III, Session 2 contrasts are stated in Table IV, and Session 3 contrasts appear in Table V. All coordinates (x, y, and z) are reported in MNI space. Only significant striatal activations are reported in the text below. Regions of significant activation outside of the striatum are presented in Tables III–V. FMRI contrasts of interest are displayed in Figures 6 and 7.

Session 1

Session 1 was divided into two phases of learning based on behavioral performance. Phase 1 included Blocks 1–3, whereas Phase 2 comprised Blocks 4–12. During Phase 1, RTs were longer and accuracy was slightly lower, with greater across-trial variability in these measures than in

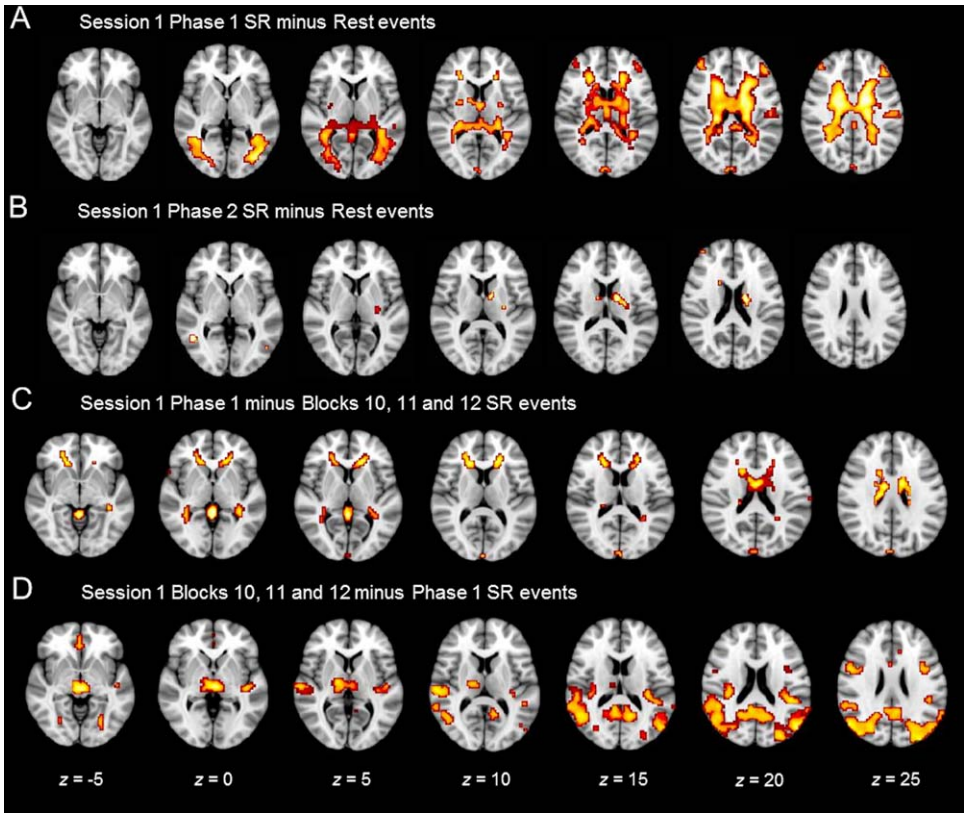

Figure 6.

Significant activations in contrasts of interest in Session 1 Phases 1 (i.e., Blocks 1–3) and 2 (i.e., Blocks 4–12): SR events. The figure shows significant activation at a threshold of $q < 0.05$ corrected for false discovery rate (FDR). In each contrast of interest, horizontal slices are presented ranging from $z = -5$ to $z = 25$, every 5 mm. (**A**) BOLD signal for stimulus-response minus rest events in Phase 1 of Session 1. (**B**) BOLD signal for stimulus-response minus rest events in Phase 2 of Session 1. (**C**) BOLD signal for Phase 1 minus Blocks 10, 11, and 12 of Session 1 stimulus-response events. (**D**) BOLD signal for Blocks 10, 11, and 12 of Session 1 minus Phase 1 stimulus-response events. SR, stimulus-response events. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE III. Significant brain activations in Session 1 contrasts of interest reported in MNI space in the Main Experiment

Contrast	Anatomical area	Cluster size	*t*	*q*	*x*, *y*, *z*
Session 1: Phase 1					
SR minus rest	**Left dorsal caudate nucleus**	1108	6.37	<0.001	−18, −1, 25
	Right dorsal caudate nucleus	*	5.54	<0.001	21, −4, 25
	Right occipital fusiform gyrus	5836	7.67	<0.001	48, −64, −20
	Left occipital pole	239	5.76	0.006	0, −97, 16
	Left postcentral gyrus	139	3.93	0.028	−45, −37, 61
FB minus rest	No suprathreshold activations				
SR minus FB	**Left dorsal caudate nucleus**	152	5.29	0.003	−15, 11, 25
	Right dorsal caudate nucleus	*	3.59	0.028	18, −19, 25
	Right occipital pole	207	6.34	0.001	3, −91, 22
	Right inferior frontal gyrus	72	4.35	0.026	54, 17, −2
FB minus SR	Left juxtapositional lobule cortex	23	5.33	0.020	−6, −1, 58
	Left middle frontal gyrus	23	5.29	0.020	−30, −4, 52
Session 1: Phase 2					
SR minus rest	**Left ventral putamen**	67	3.58	<0.001	−24, 2, −10
	Right lateral occipital complex	79	4.59	0.022	51, −64, −14
	Right cerebellum	208	4.37	0.001	33, −52, −29
	Left cerebellum	214	4.26	0.001	−39, −61, −23
FB minus rest	No suprathreshold activations				
SR minus FB	**Right ventral putamen**	*	4.54	0.017	24, 8, −11
	Left supramarginal gyrus	1388	5.28	<0.001	−60, −31, 46
	Left lateral occipital cortex	346	5.10	<0.001	−48, −70, −14
	Right insular cortex	560	4.96	<0.001	39, −1, −2
	Right cuneal cortex	732	4.68	<0.001	0, −79, 25
	Right supramarginal gyrus	251	4.56	<0.001	60, −31, 40
	Right middle frontal gyrus	137	4.55	0.004	36, 35, 43
	Left frontal pole	115	4.48	0.007	−42, 44, 28
	Right middle temporal gyrus	332	4.27	<0.001	51, −52, −2
FB minus SR	No suprathreshold activations				
Session 1: Phase 1 versus Phase 2 for SR events					
Phase 1 minus Blocks 4–6	No suprathreshold activations				
Blocks 4–6 minus Phase 1	Left cingulate gyrus	165	5.08	0.013	−15, −28, 40
	Right parietal operculum cortex	1519	4.43	<0.001	57, −31, 31
	Left insular cortex	855	4.40	<0.001	−30, 29, 7
	Left parietal operculum cortex	355	4.25	0.001	−51, −40, 22
	Right cingulate gyrus	502	4.24	<0.001	9, 14, 34
	Right precuneous cortex	191	4.10	0.008	9, −43, 49
	Left intracalcarine cortex	890	4.01	<0.001	−9, −64, 13
	Right middle frontal gyrus	113	3.88	0.035	27, 35, 28
Phase 1 minus Blocks 7–9	**Right dorsal caudate nucleus**	267	3.69	<0.001	21, 19, 26
	Left dorsal caudate nucleus	*	3.65	<0.001	−18, 2, 26
	Left precuneous cortex	7451	5.10	<0.001	−9, −64, 16
	Right frontal medial cortex	196	4.57	0.016	6, 35, −14
Blocks 7–9 minus Phase 1	No suprathreshold activations				
Phase 1 minus Blocks 10–12	**Right dorsal caudate nucleus**	113	4.25	0.013	18, 26, 13
	Left dorsal caudate nucleus	*	4.18	0.004	−12, −1, 25
	Right lateral occipital cortex	969	5.58	<0.001	45, −70, −20
Blocks 10–12 minus Phase 1	Left precentral gyrus	2454	5.99	<0.001	−30, −7, 52
	Left lateral occipital cortex	1539	4.72	<0.001	−51, −73, 19
	Left thalamus	218	4.62	0.005	−3, −19, 1
	Right frontal medial cortex	151	4.21	0.016	3, 38, −14
	Left planum temporale	142	3.86	0.019	−33, −31, 16

Cluster size is reported in voxels. *Q* values are reported at a significance level of $q < 0.05$ corrected for false discovery rate (FDR) at the Voxel level. *T* values are reported at the voxel level. Coordinates are reported in MNI space. Striatal regions are presented first and highlighted in each contrast. SR, stimulus-response events; FB, feedback events. *Cluster size unobtainable as peak coordinates are within a larger cluster.

TABLE IV. Significant brain activations in Session 2 contrasts of interest reported in MNI space in the Main Experiment

Contrast	Anatomical area	Cluster size	*t*	*q*	*x*, *y*, *z*
Block 1 minus rest	**Right dorsal caudate nucleus**	42	3.98	<0.001	15, 1, 26
	Left dorsal caudate nucleus	85	4.08	<0.001	−18, −4, 23
	Right ventral putamen	151	4.36	<0.001	24, 14, 2
	Left ventral putamen	*	4.32	<0.001	−27, 8, −1
Block 2–8 minus rest	Right cerebellum	54	5.31	0.013	−45, −52, −32
Block 1 minus Block 8	**Right dorsal caudate nucleus**	*	3.98	<0.001	18, −4, 23
	Left dorsal caudate nucleus	23	4.26	<0.001	−18, −4, 23
	Right cerebellum	293	5.17	<0.001	27, −40, −32
	Left thalamus	160	4.65	<0.001	−6, −1, 1
	Left temporal occipital fusiform cortex	173	4.62	<0.001	−39, −58, −23
	Right superior temporal gyrus	67	4.28	0.009	42, −34, 4
	Right occipital pole	57	4.21	0.014	15, −100, 10
	Left postcentral gyrus	35	4.01	0.047	−30, −19, 37
Block 8 minus Block 1	No suprathreshold activations				

Cluster size is reported in voxels. *Q* values are reported at a significance level of $q < 0.05$ corrected for false discovery rate (FDR) at the Voxel level. *T* values are reported at the voxel level. Coordinates are reported in MNI space. Striatal regions are presented first and highlighted in each contrast. SR, stimulus-response events; FB, feedback events. *Cluster size unobtainable as peak coordinates are within a larger cluster.

Phase 2, reflecting response deliberation. During Phase 2, RTs and accuracy had stabilized, indicating that the stimulus–response associations were well-learned and required less consideration at this stage. Session 1 contrasts of interest are reported in Table III.

Stimulus–response decisions: Phase 1, Session 1. In Phase 1, significant activation occurred in the left (*peak coordinates*: −18, −1, 25; $t = 6.37$; $q < 0.001$), and right (*peak coordinates*: 21, −4, 25; $t = 5.54$; $q < 0.001$) dorsal caudate nucleus contrasting stimulus–response events with rest periods (Fig. 6A). Significant activation also occurred in the left (*peak coordinates*: −15, −1, 25; $t = 5.29$; $q = 0.003$) and right (*peak coordinates*: 18, −19, 25; $t = 3.59$; $q = 0.028$) dorsal caudate nucleus contrasting stimulus–response minus feedback events.

Receiving feedback: Phase 1, Session 1. No significant striatal activations arose for feedback events minus rest or stimulus–response events.

Stimulus–response decisions: Phase 2, Session 1. Significant activation occurred in the left ventral putamen (*peak coordinates*: −24, 2, −10; $t = 3.58$; $q < 0.001$) for Phase 2 stimulus–response events minus rest (Fig. 6B). In addition, significant activation occurred in the right ventral putamen for stimulus–response events minus feedback events (*peak coordinates*: 24, 8, −11; $t = 4.54$; $q = 0.017$). To further explore Phase 2, stimulus–response events were compared to rest at a more liberal criterion of $P < 0.005$ uncorrected for multiple comparisons with a cluster threshold of 10 contiguous voxels. Even using this liberal criterion, no peaks in the DS were revealed. Some activation related to the peak in the left ventral putamen extended dorsally into DS but only at this lessened criterion (*peak coordinates*: −27, 5, −7; $t = 3.70$; $P < 0.001$).

Receiving feedback: Phase 2, Session 1. No significant activation occurred during Phase 2 for feedback events minus rest, or feedback minus stimulus–response events.

TABLE V. Significant brain activations in Session 3 contrasts of interest reported in MNI space in the Main Experiment

Contrast	Anatomical area	Cluster size	*t*	*P*	*x*, *y*, *z*
Facilitation (Congruent minus Control)	No suprathreshold activations				
Control minus Congruent	No suprathreshold activations				
Interference (Incongruent minus Control)	No suprathreshold activations				
Control minus Incongruent	No suprathreshold activations				
Incongruent minus Congruent	No suprathreshold activations				
Congruent minus Incongruent	No suprathreshold activations				
Congruent and Incongruent minus Control	**Left dorsal putamen**	**271**	**2.86**	**0.003**	**−18, −13, 14**
Control minus Congruent and Incongruent	No suprathreshold activations				

Cluster size is reported in voxels. *P* values are reported at a significance level of $P < 0.005$ uncorrected for multiple comparisons. *T* values are reported at the voxel level. Coordinates are reported in MNI space. Striatal regions are presented first and highlighted in each contrast. Facilitation was calculated as mean RTs in the congruent minus control condition and interference was calculated as mean RTs in the incongruent minus control condition.

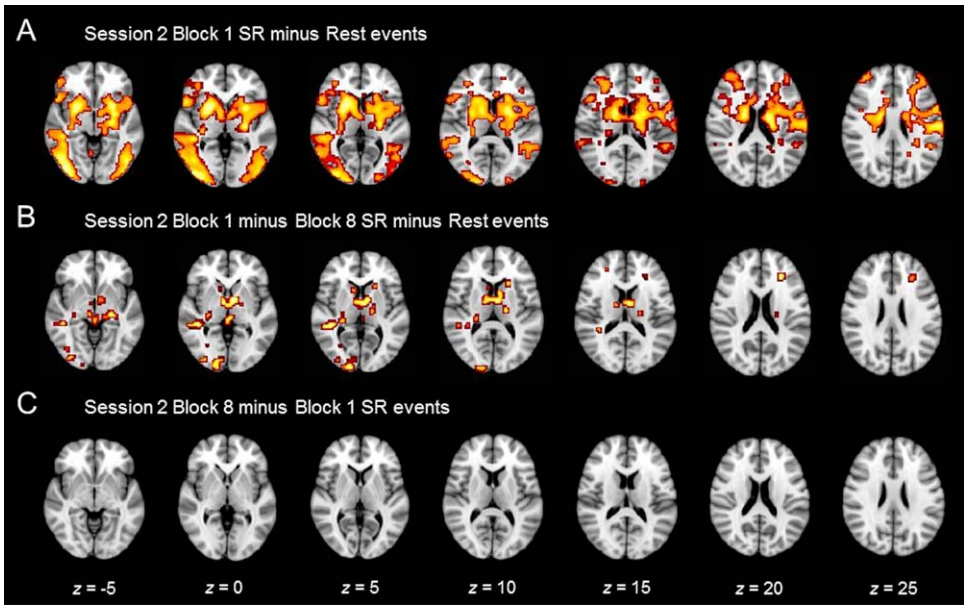

Figure 7.

Significant activations in contrasts of interest in Session 2. The figure shows significant activation at a threshold of $q < 0.05$ corrected for false discovery rate (FDR). In each contrast of interest, horizontal slices are presented ranging from $z = -5$ to $z = 25$, every 5 mm. (**A**) BOLD signal for stimulus-response events of Block 1 of Session 2 minus rest. (**B**) BOLD signal for stimulus-response events of Block 1 minus Block 8 of Session 2. (**C**) BOLD signal of stimulus-response events of Blocks 8 minus Blocks 1 of Session 2. SR, stimulus-response events. [Color figure can be viewed at wileyonlinelibrary.com]

Stimulus–response decisions: Phase 1 versus Phase 2. Given that Phase 1 consisted of the first three blocks and Phase 2 was composed of the last nine blocks (Block 4–12), contrasts were made between Phase 1 and Phase 2, grouped into three consecutive blocks, to create balanced contrasts. No significant striatal activations occurred in the Phase 1 minus Blocks 4, 5, and 6 contrast, or the reverse contrast. Significant activation arose in the left and right dorsal caudate nucleus (*peak coordinates*: −18, 2, 26; $t = 3.65$; $q < 0.001$, and *peak coordinates*: 21, −19, 26; $t = 3.69$; $q < 0.001$, respectively), for Phase 1 minus Blocks 7, 8, and 9, and for Phase 1 minus Blocks 10, 11, and 12 (*peak coordinates*: −12, −1, 25; $t = 4.18$; $q = 0.004$, and *peak coordinates*: 18, 26, 13; $t = 4.25$; $q = 0.013$, respectively; Fig. 6C) contrasts. No significant striatal activation occurred during the reverse contrasts (Fig. 6D).

Session 2

Session 2 contrasts of interest are reported in Table IV.

Stimulus–response decisions: Block 1, Session 2. Significant activation arose in the left (*peak coordinates*: −18, −4, 23; $t = 4.08$; $q < 0.001$), and right (*peak coordinates*: 15, 1, 26; $t = 3.98$; $q < 0.001$) dorsal caudate nucleus, and left (*peak coordinates*: −27, 8, −1; $t = 4.32$; $q < 0.001$) and right (*peak coordinates*: 24, 14, 2; $t = 4.36$; $q < 0.001$) ventral putamen, when Block 1 decision events were contrasted with rest periods (Fig. 7A). No significant striatal activation arose for each of Blocks 2–8 when compared with rest events at $q < 0.05$ FDR or even using a more liberal criterion of $P < 0.005$ uncorrected for multiple comparisons. Significant activation in left and right dorsal caudate nucleus arose when stimulus response events in Block 1 were contrasted with those in Block 8 of Session 2 (*peak coordinates*: −18, −4, 23; $t = 4.26$; $q < 0.001$ and *peak coordinates*: 18, −4, 23; $t = 3.98$; $q < 0.001$, respectively; Fig. 7B,C).

Session 3

Session 3 contrasts of interest are reported in Table V.

Localization responses: There were no significant activations in any striatal regions for contrasts of facilitation (i.e., congruent minus control trials), interference (i.e., incongruent minus control trials), or incongruent and congruent vs. control trials at an FDR corrected threshold of $q < 0.05$. At a less stringent threshold of $P < 0.005$ uncorrected, however, contrasting incongruent and congruent trials (i.e., conditions in which suppression of previously learned stimulus-identity responses were required in favor of the less-practiced location responses) with control trials (i.e., condition in which there were no previously-learned stimulus-identity responses to distract from location responses), a 271 voxel cluster in left dorsal putamen

extending into dorsal caudate nucleus appeared (*peak coordinates*: −18, −13, 14; $t = 2.86$; $P < 0.003$).

Bayesian analysis

Beta values in the bilateral dorsal caudate nucleus ROI were extracted for stimulus–response events separately for Sessions 1, 2, and 3. These values were used in the Bayesian analysis. To rule out a role for DS in late stimulus–response learning, DS BOLD signal was predicted to attenuate, despite behavioral signs of ongoing late-stage learning, during Phase 2, Session 1, and Blocks 2–8, Session 2. Bayes' factor one-sample *t* tests were conducted on the beta values extracted from the dorsal caudate nucleus ROIs in these sessions. In this Bayesian analysis, a Bayes' factor of <3 is considered to significantly support the null hypothesis [Dienes, 2014] that DS activation was not correlated with stimulus–response events.

Session 1 Bayes' factors: Bayes' factor one-sample *t* tests were conducted separately on the average beta values for each block in Session 1. As supported in the whole brain analysis, Bayes' factors in Blocks 1–4 significantly supported the alternative hypothesis that activation in DS in these blocks is significantly greater than zero. Blocks 5–12, however, all had a Bayes' factor of less than 3, indicating that the beta values in DS are not greater than zero, strongly supporting the null hypothesis. That is, in Session 1, DS appears to mediate response-selection responses in Phase 1 (i.e., Blocks 1–3), with values ranging from 7.2 to 15.4, and in Block 4, with a Bayes' factor of 8.5. These results strongly support the alternative hypothesis. For all subsequent blocks in Session 1, Bayes' factors were well below the cut-off of 3, with a mean Bayes' factor of 1.12 (0.09) in all blocks but one. In Block 10 only, an isolated finding, the DS Bayes' factor trended toward being greater than zero ($BF_{10} = 2.78$). Entirely, consistent with the frequency-based statistical analyses, our Bayesian analysis of these data strongly support the view that DS BOLD signal preferentially arises during blocks when response deliberation is expected based on serial order positions, and confirmed by RT, accuracy, and the variability of behavior across trials.

Session 2 Bayes' factors: A similar Bayesian analysis was conducted on each of the eight average block beta values extracted from the DS ROI. Supporting the Session 2, whole brain analysis, only the first block was trending towards being significantly greater than zero ($BF_{10} = 2.61$). Blocks 2–8 had Bayes' factors of <1, with a mean Bayes' factor of 0.20 (0.01), strongly supporting the null hypothesis, that the average DS beta values are not significantly greater than zero. That is, DS is neither mediating learning or responding in these later sessions when responses were relatively effortless and therefore required less reflection.

Session 3 Bayes' factors: Similar to the above Bayesian analyses for Sessions 1 and 2, beta values were extracted from the bilateral DS ROIs for each of the congruent, incongruent, and control regressors. Bayes' factor, one-sample *t* tests were conducted on facilitation (i.e., congruent minus control trials) and interference (i.e., incongruent minus control trials) scores. All scores had a Bayes' factor of <1.5 indicating that for facilitation ($BF_{10} = 1.30$), interference ($BF_{10} = 0.46$), and for the sum of congruent and incongruent minus control ($BF_{10} = 0.62$), DS activity beta values are not significantly greater than zero using this analysis.

DISCUSSION

Examining late-stage stimulus–response learning, we found that DS activity—specifically the body of dorsal caudate nucleus—correlated with deliberate decision-making rather than feedback events, replicating our main finding in Hiebert et al. [2014b]. We divided Session 1 into Phases 1 and 2, guided by the serial order of blocks and based on behavioral data. We examined Phases 1 versus 2 of Session 1, and Block 1 versus 2–8 of Session 2 separately because the concepts that DS mediates (a) learning stimulus–response associations to the point of automaticity versus (b) deliberate response selections, predict different patterns of DS engagement during earlier versus later trials of Session 1 and in the initial block of Session 2 compared to later blocks.

Significant DS activity occurred during stimulus–response events in Phase 1, Session 1, but not Phase 2, Session 1. These findings held whether stimulus–response events in Phase 1 and 2 were contrasted with rest periods, with feedback periods, or with one another. This is important because stimulus–response automaticity had not been achieved at the end of Session 1, attested to by improved RT and differences in BOLD signal across Phase 2, Session 1 to Session 2. Furthermore, pairwise comparisons across blocks in Session 1 continued to reveal small but significant differences in RT throughout, though SD and accuracy had plateaued. Evidence that stimulus–response automaticity was achieved only occurred by the end of Session 2, given (a) increased errors in the incongruent relative to the control conditions, (b) a trend toward significant interference (i.e., incongruent minus control) in terms of RT data, and (c) significant DS activation (i.e., dorsal putamen extending into dorsal caudate nucleus), in a location-based Stroop task in Session 3. If DS mediates learning to the point of automaticity, DS activation should persist until this process is complete. DS BOLD signal dropped out well before this point, demonstrating dissociation between DS BOLD signal and the progression of stimulus–response association automatization. DS activation was significantly greater for stimulus–response events in Phase 1, Session 1, relative to Phase 2, Session 1 (i.e., Blocks 7–9; 10–12). The correspondence of DS activity with stimulus–response decisions in Phase 1, when longer RTs, lower accuracy, and greater trial-by-trial variability (i.e., SD) occurred, relative to when more stable responding

occurred in Phase 2, was entirely in keeping with its proposed role in deliberate decision making.

The main aim of Session 2, and the 20-min distractor task that occurred prior to it, was to create situations in which predictions regarding DS activation levels would differ for the competing accounts of DS's role in cognitive function. Further, Session 2 was designed to evaluate whether automaticity had been achieved by the end of Session 1. This would be suggested by an absence of change in (a) behavior (i.e., RT, SD, or accuracy) and (b) BOLD signal from Phase 2, Session 1 to Session 2, despite an intervening period of distraction. As detailed above, this was not the case. Further, the distractor period was intended to reintroduce some uncertainty and hence deliberation in response-selection decisions. If DS mediates deliberate response selections, generating uncertainty was expected to cause an increase or re-engagement of DS activity initially in Session 2 (i.e., in Block 1), until participants refamiliarized themselves once more with stimulus-specific responses. Supporting the view that DS mediates deliberate, response decisions, DS BOLD signal re-emerged and correlated with stimulus–response events in Block 1 of Session 2 only. This block occurred immediately following a 20-min, unrelated distractor task. DS BOLD signal did not correlate preferentially with stimulus–response decisions in Blocks 2–8 of Session 2 compared to rest. Further, significantly greater DS BOLD signal resulted comparing Block 1, immediately following distraction, to Block 8, at the end of Session 2.

Using fMRI in healthy controls, we can only contradict the entrenched view that DS mediates development of stimulus–response automaticity by demonstrating absence of DS BOLD signal despite behavioral evidence that stimulus–response automatization remained in progress (i.e., a null result). That is, this claim would be challenged by dissociating neural signal in DS and behavioral signs of learning. There is a, perhaps, justified bias against publishing null effects. Null effects can have multiple interpretations including the possibility that a true difference was not detected due to insensitivity of measures or related to lack of statistical power (i.e., Type II error). Further with frequentist approaches, the null and the alternative hypotheses are set up to be asymmetric with investigator control of the maximum error allowable for supporting the alternative hypothesis whereas the error associated Type II errors varies in each study based on experimental features and power [Dienes, 2014]. The application of Bayesian analysis can reduce pitfalls in dealing with negative results and interpreting null effects. Bayesian analysis treats null and alternative hypotheses symmetrically, using the data themselves to determine the relative fit to the respective models. In this way, the statistical obstacles and validity of accepting versus rejecting the null hypotheses are equated with Bayesian analysis [Dienes, 2014].

We performed Bayesian analysis on average block beta values extracted from bilateral DS, specifically the dorsal caudate nucleus ROIs. These ROIs were defined using the anatomical boundaries of the caudate nucleus above $z = 2$ mm. There was significant support for dorsal caudate nucleus BOLD greater than zero in Phase 1, Session 1, as well as in in Block 4 (i.e., the first block of Phase 2), Session 1. Bayesian analysis significantly supported accepting the null hypothesis that activation of DS activation was not greater than zero in all blocks save Block 4 of Phase 2, Session 1. Frequency-based analyses revealed significant re-emergence of dorsal caudate nucleus activation in Block 1, Session 2. The Bayes' Factor only trended toward significance for Block 1, Session 2 (i.e., 2.61 with significance threshold set at 3), not fully supporting the alternative hypothesis. It is notable, however, that the mean Bayes' factors for all other blocks in Session 2 (i.e., Blocks 2–8) was 0.20. This pattern of results is entirely incompatible with the view that DS mediates late-learning to the point of automaticity and wholly supports the notion that DS underlies decisions that still require reflection.

Supplemental Experiment 2

Based on improved RT and differences in BOLD signal from Phase 2, Session 1 to Session 2, automaticity was not achieved at the end of Session 1 let alone at the end of Phase 1, Session 1. Nonetheless, DS signal had dropped out by Phase 2 (i.e., across Blocks 5–12), Session 1. Significant DS BOLD signal was noted only in Phase 1 (i.e., Blocks 1–3, and Block 4, the latter was only revealed using Bayesian analyses), Session 1 when RT, error rates, and mean block SDs were high, suggesting deliberation. Preferential DS BOLD signal also occurred in Block 1, Session 2, following a 20-min distractor task aimed at reintroducing uncertainty and some consideration of response selection decisions. Phase 1, Session 1 constituted only 9 presentations of each stimulus, which referring to the larger literature would be insufficient to support the development of automatic stimulus-specific responding [Foerde et al., 2006; Helie et al., 2010; MacLeod and Dunbar, 1988; Myers et al., 2003; Poldrack et al., 2005; Shiffrin and Schneider, 1977; Shohamy and Wagner, 2008; Wachter et al., 2009]. Nonetheless, to be entirely certain of our interpretations of the Main Experiment, we conducted Experiment 2 (Methods and Results presented in Supporting Information). In this behavioral experiment, we included a location Stroop task immediately after Phase 1, Session 1 (i.e., Session 3A) and at the end of Session 2 (i.e., Session 3B), to directly rule out the possibility that stimulus–response automaticity had been achieved after Phase 1.

Performance in Sessions 1 and 2 of Experiment 2 entirely replicated behavioral findings in our Main Experiment (i.e., compare Fig. 5 and Supporting Information, Fig. 1). Significant interference in location responses using RT or accuracy did not occur in the incongruent relative to the control condition in Session 3A. Similarly, there was not significant RT or accuracy facilitation in the congruent

relative to the control condition in Session 3A. Consequently, there was no evidence that stimulus-specific responses had achieved automatic status at the conclusion of Phase 1, Session 1, based on performance of a modified location Stroop task in Session 3A. There was a trend toward slower RTs in Block 1, Session 2, relative to Block 12, Session 1, replicating the finding in our Main Experiment that stimulus–response automaticity was not achieved by the end of Session 1.

In contrast, significant interference in terms of RT occurred during Session 3B, after stimulus–response associations had been trained in Session 1 (i.e., 12 blocks), and Session 2 (i.e., 8 blocks), for incongruent relative to control trials. This suggests that stimulus–response automaticity was achieved by the end of Session 2, entirely consistent with our findings in the Main Experiment.

The results in Experiment 2 inform our interpretation of the fMRI findings in the Main Experiment. Taken together, the results favor the view that DS activation correlated with stimulus–response events in Phase 1, Session 1, when an element of deliberation remained, because this region has a role in decision making, as has been suggested by others as well [Ali et al., 2010; Cools and D'Esposito, 2011; Daniel et al., 2010; MacDonald et al., 2011; Ohira et al., 2010].

Summary

Automaticity is variously defined as reflecting stimulus-specific responses that (a) persist even when feedback is omitted or is reversed, generalizing across situations [Myers et al., 2003; Shohamy and Wagner, 2008], (b) are unaffected by distracting information or tasks [Foerde et al., 2006], and (c) interfere with enacting new incongruent responses [MacLeod and Dunbar, 1988]. DS has been implicated in the development of automatic stimulus-specific responses [Ashby et al., 2010; Tricomi et al., 2009; Yin and Knowlton, 2006]. DS has also been ascribed a role in decision making when deliberation is required [Ali et al., 2010; Cools and D'Esposito, 2011; Daniel et al., 2010; DeGutis and D'Esposito, 2007; MacDonald et al., 2011; Ohira et al., 2010; Robertson et al., 2015]. Our results refute a role for DS in late-stage, stimulus–response learning and automatization, and rather are entirely consistent with the view that DS mediates deliberate decision making.

In this experiment, significant DS activity— particularly the body region of the dorsal caudate nucleus—occurred only during stimulus–response, and not feedback events, replicating our main finding in Hiebert et al., [2014b] suggesting that DS mediates response decisions and not learning from feedback. Further supporting a role for DS in mediating decisions, DS was significant in Phase 1, Session 1, when longer RTs, lower accuracy, and greater trial-by-trial variability suggested a degree of indecision and hence deliberation was required. Session 2 was performed following a 20-min distractor task that aimed to reintroduce some uncertainty in response-selection decisions. This provided a further test of the hypothesis that DS mediates decision making when choosing among response alternatives demands some contemplation of options. As we had predicted, we observed a transient re-emergence of DS activation, correlating with the decision-making events in Block 1, Session 2, immediately following distraction. In contrast, during Phase 2, Session 1, and Blocks 2–8 of Session 2, stimulus–response decisions did not correlate significantly with DS BOLD signal. Further, Bayesian analysis supported these null results in all but Block 4 (i.e., the first block) of Phase 2, Session 1. In our Main Experiment, stimulus–response automaticity had not been achieved at the conclusion of Session 1 based on the evidence that RTs and BOLD signal differed from Block 12, Session 1 and Block 1, Session 2 and the additional finding that pairwise *t*-tests of RT for individual blocks across Session 1 continued to shorten slightly across blocks. Stimulus–response associations were overlearned to the point of automaticity at the conclusion of Session 2, supported by the finding that stimulus–response associations learned in Session 1 and reinforced in Session 2 facilitated congruent and interfered with incongruent location responses in a modified location Stroop task. In Experiment 2, we sought direct evidence that Phase 1, Session 1 was not sufficient to promote development of stimulus–response automaticity, using our location Stroop task (see Supporting Information). Experiment 2 revealed that stimulus–response automaticity was not achieved following Blocks 1–3, Session 1 (i.e., Phase 1) after only 9 presentations of each stimulus. The fact that DS activation attenuated after Phase 1, Session 1, before automaticity was achieved, in the Main Experiment is therefore wholly inconsistent with the contention that DS mediates late-stage, stimulus–response learning to the point of automaticity [Ashby et al., 2007; Balleine and O'Doherty, 2010; Yin and Knowlton, 2006]. There was a clear dissociation between DS BOLD signal and behavioral evidence of late-stage, stimulus–response association automatization.

In contrasts where DS activation emerged significantly, cortical regions previously implicated in decision making and categorization judgments were also revealed. These included occipital regions of the fusiform gyrus that have been implicated in decision making, specifically in motor planning and execution [Tosoni et al., 2016], and the occipital pole and lateral occipital cortex that are both implicated in object recognition [Vernon et al., 2016]. Object recognition is a required step toward enacting stimulus-specific response selections. The right inferior frontal gyrus has been shown to implement and reprogramme action plans [Stock et al., 2016]. Many of the brain regions that were significantly activated along with DS during response-selection events are reciprocally connected with the dorsal caudate nucleus, the body specifically, such as the precentral, postcentral, inferior, and fusiform gyri [Robinson et al., 2012; Tziortzi et al., 2014]. These results

highlight the fact that, whereas the DS does not function in isolation, it plays a key, central role in performing response-related decisions.

DS in Stimulus–Response Learning Versus Decision Making

The claim that DS mediates learning is well-entrenched [Ashby et al., 2007, 2010; Balleine et al., 2009; Brovelli et al., 2011; O'Doherty et al., 2004; Yin and Knowlton, 2006]. Challenges to this notion are accruing, however [Atallah et al., 2007; Exner et al., 2002; MacDonald et al., 2013a; Vo et al., 2014]. In a previous experiment, we investigated DS's role in *early* stimulus–response learning. We found that DS activity, particularly the head of dorsal caudate nucleus, correlated with stimulus–response decisions and enactment, not with feedback processing, the point at which early, stimulus–response associations are learned [Hiebert et al., 2014b]. In that experiment, DS activity did not correlate with response decisions in the first half of our session, before response tendencies had developed. DS activity emerged and correlated significantly with stimulus–response decisions in later stages of stimulus–response learning. At these later stages, when DS activity correlated with stimulus–response events, the learning curve was shallower and therefore DS did not seem to be tracking learning behavior *per se*. Furthermore, and quite convincing that DS does not mediate early, stimulus–response learning via feedback, DS preferentially correlated with stimulus–response decision events in Session 2, when feedback was omitted and hence further feedback-based learning was precluded. In Session 2, however, decision accuracy remained imperfect (i.e., mean 92%), and RTs (i.e., mean 696 ms) suggested some deliberation was required. That is, DS activity arose when stimulus-specific responses were not overlearned and still required a degree of deliberation in this session of our previous experiment. We argued that DS is erroneously implicated in stimulus–response learning because it mediates aspects of decision making, and most stimulus–response learning studies combine decision and learning processes. This confound exists at the behavioral level in that expression of learning typically depends on intact decision-making abilities. In neuroimaging studies, neural activation associated with learning and decision processes are frequently merged into a single *learning* event. Though our previous finding seriously challenged the premise that DS mediates early stimulus–response learning, we could not comment on the DS's role in late-stage learning, particularly in stimulus–response automaticity that occurs through repeated experience of stimulus–response associations and does not necessarily depend upon feedback. The view that DS mediates late learning is also prevalent [Ashby et al., 2010; Balleine et al., 2009; Ruge and Wolfensteller, 2013; Tricomi et al., 2009] and this served as the impetus for the Main Experiment.

Extending our previous investigation [Hiebert et al., 2014b], here we examined DS's role in late-stage learning versus decision making. Our results were entirely consistent with the view that DS mediates decisions when a degree of deliberation is required (Session 1, Phase 1; Session 2, Block 1), consistent with our previous conclusions regarding DS's role in an early-learning experiment [Hiebert et al., 2014b]. That DS activity attenuated *before* automaticity had been achieved is inconsistent with the view that it mediates late-stage stimulus–response learning [Balleine and O'Doherty, 2010; Helie et al., 2010; Liljeholm and O'Doherty, 2012; Macpherson et al., 2014; Soto et al., 2013; Voorn et al., 2004; Yin and Knowlton, 2006]. If the role of DS is to learn stimulus–response associations and to train cortical-cortical connections to the point of automaticity, DS activity should have persisted into Session 2, given that this learning process had not reached completion based on differences in RT and BOLD signal from Session 1 to Session 2 [Ashby et al., 2007]. The current results are therefore at odds with the SPEED model ascribing DS a role in mediating automaticity [Ashby et al., 2007; Helie et al., 2010] and with the theory that DS not only mediates stimulus–response habit learning but also underlies responding that is habitual [Balleine and O'Doherty, 2010; Everitt and Robbins, 2005].

The finding that DS activity for stimulus–response events attenuates prior to the development of automatic responding has been shown convincingly by others as well [Wu et al., 2004; Waldschmidt and Ashby, 2011; Soto et al., 2013]. de Wit et al. [2011] used an instrumental conflict task, where participants first learned simple biconditional associations in a goal-directed or habit fashion, and later performed decisions where select outcomes were devalued. Patients with PD, tested in the OFF or ON dopaminergic medication states, scored similarly to controls in the outcome-devalued stage of the experiment with respect to both the goal-directed and habit learned associations. In PD, DS is significantly dopamine depleted and hence DS functions a significantly impaired in the off state and is improved by dopaminergic therapy. These findings, therefore suggest that DS does not mediate the development of automaticity, or interestingly even goal-directed learning in this task [de Wit et al., 2011].

More consistent with our current results, and with our previous findings [Hiebert et al., 2014b], DS seems to be implicated in decision making only once stimulus–response tendencies begin to develop, when a degree of deliberation remains, but before responses are enacted with little reflection or automatically (Fig. 7). These results integrate with a growing literature linking DS to decision making [Atallah et al., 2007; Grahn et al., 2008], particularly the body of the caudate nucleus. as we have shown here [Cincotta and Seger, 2007; Little et al., 2006; Seger et al., 2010], and especially when deliberation, and cognitive control or flexibility processes are required [Cools and D'Esposito, 2011; Robertson et al., 2015]. In neuroimaging

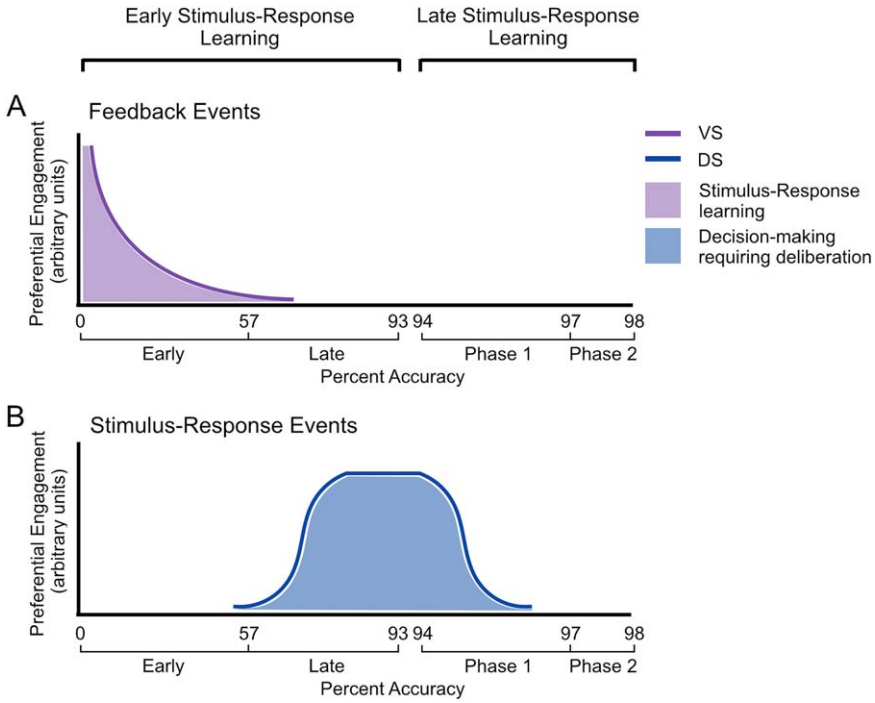

Figure 8.

Roles of DS and VS in early and late stimulus-response learning as supported by our findings in Hiebert et al. [2014b] and the Main Experiment of this study. Graphs presented above illustrate preferential patterns of DS and VS activation for stimulus-response events versus feedback separately, following the course of learning from early to late stage. This is not actual data and the amplitude and shape of curves reflect our theoretical interpretations of our results. We present Session 1 of Hiebert et al. [2014b], divided in half. Average percent accuracy achieved after the first half of Session 1 was 57%. The average percent accuracy for Session 1 final learning was 93%. For this study, percent accuracy for Block 1, Session 1 was 94%. Session 1 was divided into Phase 1 (Blocks 1–3) and 2 (Blocks 4–12). The average percent accuracy achieved at the end of Phase 1 was 97% and at the end of Phase 2 was 98%. (**A**) Activation patterns during feedback events. VS activity was noted significantly only in the first half of Session 1 [Hiebert et al., 2014b] VS was not significantly engaged during the feedback events in the Main Experiment. (**B**) Activation patterns during stimulus-response events. DS activity was noted significantly only during the second half of Session 1 and Session 2 [Hiebert et al., 2014b] when stimulus–response associations were learned but still required deliberation. In the Main Experiment, DS was only significant in Phase 1, Session 1 when response selections were learned but still required deliberation based on accuracy and RT. Preferential DS activity was not noted relative to rest, feedback, or Phase 1 stimulus–response events, for stimulus–response events during Phase 2 of Session 1 and for the bulk of Session 2. [Color figure can be viewed at wileyonlinelibrary.com]

studies, DS activity correlates with degree of category [Daniel et al., 2010], response-reward [Ohira et al., 2010], and stimulus–response [Ali et al., 2010; MacDonald et al., 2011] uncertainty. Further, investigations in patients with DS lesions and in PD patients reveal more significant impairments for decisions requiring greater deliberation and in some cases *superior performance* relative to healthy controls for choosing *more* automatic responses [Benke et al., 2003; Cameron et al., 2010; Cools et al., 2006, 2009; Hood et al., 2007; MacDonald et al., 2011; Thoma et al., 2008]. Finally, in neuroimaging studies that utilize the Stroop task, a robust paradigm that examines cognitive control [MacLeod and MacDonald, 2000] resolving response conflict and inhibiting prepotent responses in the incongruent condition frequently implicate DS [Ali et al., 2010; Coderre and van Heuven, 2013; Robertson et al., 2015]. These findings are at odds with any theory that ascribes a role to DS in habit learning or habitual responding.

Role of the Striatum in Stimulus–Response Learning and Decision Making

Figure 8 presents our theorized patterns of DS and VS engagement for stimulus–response versus feedback events separately, following the course from early- to late-stage learning and decision making, based on our previous [Hiebert et al., 2014b] and current results. In Hiebert et al.

[2014b], stimulus–response learning in Session 1 was divided in half. The first half revealed a much steeper slope of stimulus–response learning via feedback than the second. The average percent accuracy achieved after the first half of Session 1 in Hiebert et al. [2014b] was 57%. The average percent accuracy at the end of the second half of Session 1 (i.e., final learning score) was 93%. In the Main Experiment, after a period of explicit study of stimulus–response associations, the percent accuracy of the first block of trials in Session 1 was 94%. Session 1 of the current study was divided into Phases 1 (Blocks 1–3) and 2 (Blocks 4–12) based on behavioral patterns of accuracy, RT, and intertrial variability. The average percent accuracy and RT achieved at the end of Phase 1 were 97% and 746 ms and at the end of Phase 2 were 98% and 694 ms, respectively.

DS was preferentially engaged during stimulus–response events in both experiments (Fig. 8B). DS activity peaked toward the end of the learning phase in Hiebert et al. [2014b] when stimulus–response associations were beginning to form but when response selections were still somewhat uncertain (i.e., $>57\%$ accuracy). In this study, DS activity occurred early once response selections were learned but still required deliberation based on accuracy and RT (i.e., $<97\%$ accuracy). DS activity did not correlate preferentially with stimulus–response events during Phase 2 of Session 1 of the Main Experiment in which accuracy was above 97% and RTs were quite short. We conceptualize that responses during Phase 2 of Session 1 required much less consideration though they had not yet achieved automaticity based on our objective measures. These results together suggest that DS neither mediates early, feedback-based learning, nor late-stage stimulus–response automaticity. Instead, these results integrate with a growing literature implicating DS in decision making [Atallah et al., 2007; Grahn et al., 2008], particularly when deliberation is required [Cools and D'Esposito, 2011].

In contrast, VS was preferentially engaged during feedback events (Fig. 8A) in Hiebert et al. [2014b], peaking in the first half of Session 1, when the slope of learning was steepest. VS BOLD signal for feedback events was not significantly different relative to rest or stimulus–response events in the second half of Session 1 in Hiebert et al. [2014b], when slope of behavioral change indicated that learning had decreased. Consistent with this pattern, VS was not significantly engaged during the feedback events in Session 1 of this study, which focused on late learning. Early stimulus–response association learning had already occurred prior even to Block 1, Session 1 in the Main Experiment, due to an explicit learning session that preceded the fMRI portion of this study, intended as a shortcut to later learning, making feedback much less informative. Our results integrate with an emerging literature suggesting that VS mediates many forms of initial/early learning both with and without the provision of feedback, including reward learning [Camara et al., 2008; MacDonald et al., 2013a], stimulus-stimulus learning [MacDonald et al., 2011], motor learning [Feigin et al., 2003], sequence learning [Ghilardi et al., 2007], category learning [Hampshire et al., 2016; Shohamy et al., 2006], and list learning [MacDonald et al., 2013b].

CONCLUSIONS

The striatum is increasingly implicated in cognitive functions [MacDonald et al., 2014b]. We found that DS activity correlates only with decisions and response selections requiring deliberation but not with late-stage, stimulus–response association learning. Our results challenge the notion that the DS underlies the development of automaticity, integrating rather with a growing literature suggesting that DS—particularly the caudate nucleus—mediates decision making [Cincotta and Seger, 2007; Little et al., 2006; Seger et al., 2010] when an element of deliberation is required [Atallah et al., 2007; Grahn et al., 2008; Hiebert et al., 2014b; Jessup and O'Doherty, 2011; MacDonald et al., 2014a; McDonald and Hong, 2004; Postle and D'Esposito, 1999; Smittenaar et al., 2012].

REFERENCES

Ali N, Green DW, Kherif F, Devlin JT, Price CJ (2010): The role of the left head of caudate in suppressing irrelevant words. J Cogn Neurosci 22:2369–2386.

Ashby FG, Ennis JM, Spiering BJ (2007): A neurobiological theory of automaticity in perceptual categorization. Psychol Rev 114: 632–656.

Ashby FG, Turner BO, Horvitz JC (2010): Cortical and basal ganglia contributions to habit learning and automaticity. Trends Cogn Sci 14:208–215.

Atallah HE, Lopez-Paniagua D, Rudy JW, O'Reilly RC (2007): Separate neural substrates for skill learning and performance in the ventral and dorsal striatum. Nat Neurosci 10:126–131.

Balleine BW, Liljeholm M, Ostlund SB (2009): The integrative function of the basal ganglia in instrumental conditioning. Behav Brain Res 199:43–52.

Balleine BW, O'Doherty JP (2010): Human and rodent homologies in action control: Corticostriatal determinants of goal-directed and habitual action. Neuropsychopharmacology 35:48–69.

Benke T, Delazer M, Bartha L, Auer A (2003): Basal ganglia lesions and the theory of fronto-subcortical loops: Neuropsychological findings in two patients with left caudate lesions. Neurocase 9:70–85.

Boettiger CA, D'Esposito M (2005): Frontal networks for learning and executing arbitrary stimulus-response associations. J Neurosci 25:2723–2732.

Brett M, Anton JL, Valabregue V, Poline JB (2002): Region of interest analysis using an SPM toolbox. Presented at the Eighth International Conference on Functional Mapping of the Human Brain, Sendai, Japan, June.

Brovelli A, Nazarian B, Meunier M, Boussaoud D (2011): Differential roles of caudate nucleus and putamen during instrumental learning. NeuroImage 57:1580–1590.

Brown TI, Stern CE (2013): Contributions of medial temporal lobe and striatal memory systems to learning and retrieving overlapping spatial memories. Cereb Cortex 1–17.

Camara E, Rodriguez-Fornells A, Munte TF (2008): Functional connectivity of reward processing in the brain. Front Hum Neurosci 2:19.

Cameron IG, Watanabe M, Pari G, Munoz DP (2010): Executive impairment in Parkinson's disease: Response automaticity and task switching. Neuropsychologia 48:1948–1957.

Cincotta CM, Seger CA (2007): Dissociation between striatal regions while learning to categorize via feedback and via observation. J Cogn Neurosci 19:249–265.

Coderre E, van Heuven W (2013): Modulations of the executive control network by stimulus onset asynchrony in a Stroop task. BMC Neurosci 14:79.

Cools R (2006): Dopaminergic modulation of cognitive function-implications for L-DOPA treatment in Parkinson's disease. Neurosci Biobehav Rev 30:1–23.

Cools R, Altamirano L, D'Esposito M (2006): Reversal learning in Parkinson's disease depends on medication status and outcome valence. Neuropsychologia 44:1663–1673.

Cools R, D'Esposito M (2011): Inverted-U-shaped dopamine actions on human working memory and cognitive control. Biol Psychiatry 69:e113–e125.

Cools R, Lewis SJ, Clark L, Barker RA, Robbins TW (2007): L-DOPA disrupts activity in the nucleus accumbens during reversal learning in Parkinson's disease. Neuropsychopharmacology 32:180–189.

Cools R, Rogers R, Barker RA, Robbons TW (2009): Top-down attentional control in Parkinson's disease: Salient considerations. J Cogn Neurosci 22:848–859.

Daniel R, Wagner G, Koch K, Reichenbach JR, Sauer H, Schlösser RGM (2010): Assessing the neural basis of uncertainty in perceptual category learning through varying levels of distortion. J Cogn Neurosci 23:1781–1793.

de Wit S, Barker R, Dickinson A, Cools R (2011): Habitual versus goal-directed action control in Parkinson's disease. J Cogn Neurosci 23:1218–1229.

DeGutis J, D'Esposito M (2007): Distinct mechanisms in visual category learning. Cogn Affect Behav Neurosci 7:251–259.

Dienes Z (2014): Using Bayes to get the most out of non-significant results. Front Psychol 5:781.

Dobryakova E, Tricomi E (2013): Basal ganglia engagement during feedback processing after a substantial delay. Cogn Affect Behav Neurosci.

Everitt BJ, Robbins TW (2005): Neural systems of reinforcement for drug addiction: From actions to habits to compulsion. Nat Neurosci 8:1481–1489.

Exner C, Koschack J, Irle E (2002): The differential role of premotor frontal cortex and basal ganglia in motor sequence learning: Evidence from focal basal ganglia lesions. Learn Memory 9:376–386.

Feigin A, Ghilardi MF, Carbon M, Edwards C, Fukuda MD, Dhawan V, Margouleff C, Ghez C, Eidelberg D (2003): Effects of levodopa on motor sequence learning in Parkinson's disease. Neurology 60:1744–1749.

Foerde K, Knowlton BJ, Poldrack RA (2006): Modulation of competing memory systems by distraction. Proc Natl Acad Sci USA 103:11778–11783.

Foerde K, Race E, Verfaellie M, Shohamy D (2013): A role for the medial temporal lobe in feedback-driven learning: Evidence from amnesia. J Neurosci 33:5698–5704.

Garrison J, Erdeniz B, Done J (2013): Prediction error in reinforcement learning: A meta-analysis of neuroimaging studies. Neurosci Biobehav Rev 37:1297–1310.

Ghilardi MF, Feigin AS, Battaglia F, Silvestri G, Mattis P, Eidelberg D, Di Rocco A (2007): L-Dopa infusion does not improve explicit sequence learning in Parkinson's disease. Parkinsonism Relat Disord 13:146–151.

Grahn JA, Parkinson JA, Owen AM (2008): The cognitive functions of the caudate nucleus. Progr Neurobiol 86:141–155.

Grahn JA, Parkinson JA, Owen AM (2009): The role of the basal ganglia in learning and memory: Neuropsychological studies. Behav Brain Res 199:53–60.

Hampshire A, Hellyer PJ, Parkin B, Hiebert N, MacDonald P, Owen AM, Leech R, Rowe J (2016): Network mechanisms of intentional learning. NeuroImage 127:123–134.

Hart G, Leung BK, Balleine BW (2013): Dorsal and ventral streams: The distinct role of striatal subregions in the acquisition and performance of goal-directed actions. Neurobiol Learn Memory.

Helie S, Roeder JL, Ashby FG (2010): Evidence for cortical automaticity in rule-based categorization. J Neurosci 30: 14225–14234.

Hiebert NM, Seergobin KN, Vo A, Ganjavi H, MacDonald PA (2014a): Dopaminergic therapy affects learning and impulsivity in Parkinson's disease. Ann Clin Transl Neurol 1:883–843.

Hiebert NM, Vo A, Hampshire A, Owen AM, Seergobin KN, MacDonald PA (2014b): Striatum in stimulus-response learning via feedback and in decision making. NeuroImage 101: 448–457.

Hood AJ, Amador SC, Cain AE, Briand KA, Al-Refai AH, Schiess MC, Sereno AB (2007): Levodopa slows prosaccades and improves antisaccades: An eye movement study in Parkinson's disease. J Neurol Neurosurg Psychiatry 78:565–570.

Jessup RK, O'Doherty JP (2011): Human dorsal striatal activity during choice discriminates reinforcement learning behavior from the gambler's fallacy. J Neurosci 31:6296–6304.

Jueptner M, Frith C, Brooks D, Frackowiak R, Passingham R (1997): Anatomy of motor learning. II. Subcortical structures and learning by trial and error. J Neurophysiol 77: 1325–1337.

Lehericy S, Benali H, Van de Moortele PF, Pelegrini-Issac M, Waechter T, Ugurbil K, Doyon J (2005): Distinct basal ganglia territories are engaged in early and advanced motor sequence learning. Proc Natl Acad Sci USA 102:12566–12571.

Liljeholm M, O'Doherty JP (2012): Contributions of the striatum to learning, motivation, and performance: An associative account. Trends Cogn Sci 16:467–475.

Little DM, Shin SS, Sisco SM, Thulborn KR (2006): Event-related fMRI of category learning: Differences in classification and feedback networks. Brain Cogn 60:244–252.

MacDonald AA, Monchi O, Seergobin KN, Ganjavi H, Tamjeedi R, MacDonald PA (2013a): Parkinson's disease duration determines effect of dopaminergic therapy on ventral striatum function. Movement Disord 28:153–160.

MacDonald AA, Seergobin KN, Owen AM, Tamjeedi R, Monchi O, Ganjavi H, MacDonald PA (2013b): Differential effects of Parkinson's disease and dopamine replacement on memory encoding and retrieval. PLoS One 8:e74044.

MacDonald AA, Seergobin KN, Tamjeedi R, Owen AM, Provost J-S, Monchi O, Ganjavi H, MacDonald PA (2014a): Examining dorsal striatum in cognitive effort using Parkinson's disease and fMRI. Ann Clin Transl Neurol 1:390–400.

MacDonald PA, Ganjavi H, Collins DL, Evans AC, Karama S (2014b): Investigating the relation between striatal volume and IQ. Brain Imaging Behav 8:52–59.

MacDonald PA, MacDonald AA, Seergobin KN, Tamjeedi R, Ganjavi H, Provost JS, Monchi O (2011): The effect of dopamine therapy on ventral and dorsal striatum-mediated cognition in Parkinson's disease: Support from functional MRI. Brain 134:1447–1463.

MacDonald PA, Monchi O (2011): Differential effects of dopaminergic therapies on dorsal and ventral striatum in Parkinson's disease: Implications for cognitive function. Parkinson's Dis:1–18.

MacLeod CM, Dunbar K (1988): Training and stroop-like interference: Evidence for a continuum of automaticity. J Exp Psychol Learn Memory Cogn 14:126–135.

MacLeod CM, MacDonald PA (2000): Interdimensional interference in the Stroop effect: Uncovering the cognitive and neural anatomy of attention. Trends Cogn Sci 4:383–391.

Macpherson T, Morita M, Hikida T (2014): Striatal direct and indirect pathways control decision-making behavior. Front Psychol 5:1301.

Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH (2003): An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. NeuroImage 19:1233–1239.

McDonald RJ, Hong NS (2004): A dissociation of dorso-lateral striatum and amygdala function on the same stimulus-response habit task. Neuroscience 124:507–513.

Myers CE, Shohamy D, Gluck MA, Grossman S, Kluger A, Ferris S, Golomb J, Schnirman G, Schwartz R (2003): Dissociating hippocampal versus basal ganglia contributions to learning and transfer. J Cogn Neurosci 15:185–193.

Nissen SB, Magidson T, Gross K, Bergstrom CT (2016): Publication bias and the canonization of false facts. Elife 5:

O'Doherty J, Dayan P, Schultz J, Deichmann R, Friston K, Dolan RJ (2004): Dissociable roles of ventral and dorsal striatum in instrumental conditioning. Science 304:452–454.

Ohira H, Ichikawa N, Nomura M, Isowa T, Kimura K, Kanayama N, Fukuyama S, Shinoda J, Yamada J (2010): Brain and autonomic association accompanying stochastic decision-making. NeuroImage 49:1024–1037.

Poldrack RA, Prabhakaran V, Seger CA, Gabrieli JDE (1999): Striatal activation during acquisition of a cognitive skill. Neuropsychology 13:564–574.

Poldrack RA, Sabb FW, Foerde K, Tom SM, Asarnow RF, Bookheimer SY, Knowlton BJ (2005): The neural correlates of motor skill automaticity. J Neurosci 25:5356–5364.

Postle BR, D'Esposito M (1999): Dissociation of human caudate nucleus activity in spatial and nonspatial working memory: An event-related fMRI study. Cogn Brain Res 8:107–115.

Postuma RB, Dagher A (2006): Basal ganglia functional connectivity based on a meta-analysis of 126 positron emission tomography and functional magnetic resonance imaging publications. Cereb Cortex 16:1508–1521.

Rangel A, Camerer C, Montague PR (2008): A framework for studying the neurobiology of value-based decision making. Nat Rev Neurosci 9:545–556.

Rieger M, Gauggel S, Burmeister K (2003): Inhibition of ongoing responses following frontal, nonfrontal, and basal ganglia lesions. Neuropsychology 17:272–282.

Robertson BD, Hiebert NM, Seergobin KN, Owen AM, MacDonald PA (2015): Dorsal striatum mediates cognitive control, not cognitive effort per se, in decision-making: An event-related fMRI study. NeuroImage 114:170–184.

Robinson JL, Laird AR, Glahn DC, Blangero J, Sanghera MK, Pessoa L, Fox PM, Uecker A, Friehs G, Young KA, Griffin JL, Lovallo WR, Fox PT (2012): The functional connectivity of the human caudate: An application of meta-analytic connectivity modeling with behavioral filtering. NeuroImage 60:117–129.

Ruge H, Wolfensteller U (2013): Functional integration processes underlying the instruction-based learning of novel goal-directed behaviors. NeuroImage 68:162–172.

Schouppe N, Demanet J, Boehler CN, Ridderinkhof KR, Notebaert W (2014): The role of the striatum in effort-based decision-making in the absence of reward. J Neurosci 34:2148–2154.

Schultz W, Apicella P, Scarnati E, Ljungberg T (1992): Neuronal activity in monkey ventral striatum related to the expectation of reward. J Neurosci 12:4595–4610.

Seger CA, Peterson EJ, Cincotta CM, Lopez-Paniagua D, Anderson CW (2010): Dissociating the contributions of independent corticostriatal systems to visual categorization learning through the use of reinforcement learning modeling and Granger causality modeling. NeuroImage 50:644–656.

Shiffrin RM, Schneider W (1977): Controlled and automatic human information processing: II. Perceptual learning, auromatic attending, and a general theory. Psychol Rev 84:127–190.

Shohamy D, Myers CE, Geghman KD, Sage J, Gluck MA (2006): L-dopa impairs learning, but spares generalization, in Parkinson's disease. Neuropsychologia 44:774–784.

Shohamy D, Wagner AD (2008): Integrating memories in the human brain: Hippocampal-midbrain encoding of overlapping events. Neuron 60:378–389.

Smittenaar P, Chase HW, Aarts E, Nusselein B, Bloem BR, Cools R (2012): Decomposing effects of dopaminergic medication in Parkinson's disease on probabilistic action selection–learning or performance?. Eur J Neurosci 35:1144–1151.

Soto FA, Waldschmidt JG, Helie S, Ashby FG (2013): Brain activity across the development of automatic categorization: A comparison of categorization tasks using multi-voxel pattern analysis. NeuroImage 71:284–297.

Stock AK, Steenbergen L, Colzato L, Beste C (2016): The system neurophysiological basis of non-adaptive cognitive control: Inhibition of implicit learning mediated by right prefrontal regions. Hum Brain Mapp 37:4511–4522.

Thoma P, Koch B, Heyder K, Schwarz M, Daum I (2008): Subcortical contributions to multitasking and response inhibition. Behav Brain Res 194:214–222.

Tosoni A, Guidotti R, Del Gratta C, Committeri G, Sestieri C (2016): Preferential coding of eye/hand motor actions in the human ventral occipito-temporal cortex. Neuropsychologia 93:116–127.

Tricomi E, Balleine BW, O'Doherty JP (2009): A specific role for posterior dorsolateral striatum in human habit learning. Eur J Neurosci 29:2225–2232.

Tziortzi AC, Haber SN, Searle GE, Tsoumpas C, Long CJ, Shotbolt P, Douaud G, Jbabdi S, Behrens TE, Rabiner EA, Jenkinson M, Gunn RN (2014): Connectivity-based functional analysis of dopamine release in the striatum using diffusion-weighted MRI and positron emission tomography. Cereb Cortex 24:1165–1177.

Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002): Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage 15:273–289.

van Assen MA, van Aert RC, Nuijten MB, Wicherts JM (2014): Why publishing everything is more effective than selective publishing of statistically significant results. PLoS One 9:e84896.

van der Meer MA, Redish AD (2011): Ventral striatum: A critical look at models of learning and evaluation. Curr Opin Neurobiol 21:387–392.

Vernon RJ, Gouws AD, Lawrence SJ, Wade AR, Morland AB (2016): Multivariate patterns in the human object-processing pathway reveal a shift from retinotopic to shape curvature representations in lateral occipital areas, LO-1 and LO-2. J Neurosci 36:5763–5774.

Vo A, Hiebert NM, Seergobin KN, Solcz S, Partridge A, MacDonald PA (2014): Dopaminergic medication impairs feedback-based stimulus-response learning but not response selection in Parkinson's disease. Front Hum Neurosci 8:784.

Voorn P, Vanderschuren LJ, Groenewegen HJ, Robbins TW, Pennartz CM (2004): Putting a spin on the dorsal-ventral divide of the striatum. Trends Neurosci 27:468–474.

Wachter T, Lungu OV, Liu T, Willingham DT, Ashe J (2009): Differential effect of reward and punishment on procedural learning. J Neurosci 29:436–443.

Waldschmidt JG, Ashby FG (2011): Cortical and striatal contributions to automaticity in information-integration categorization. Neuroimage 56:1791–1802.

Wu T, Kansaku K, Hallett M (2004): How self-initiated memorized movements become automatic: A functional MRI study. J Neurophysiol 91:1690–1698.

Wunderlich K, Dayan P, Dolan RJ (2012): Mapping value based planning and extensively trained choice in the human brain. Nat Neurosci 15:786–791.

Yin HH, Knowlton BJ (2006): The role of the basal ganglia in habit formation. Nat Rev Neurosci 7:464–476.