

Reward-Related Responses in the Human Striatum

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ABSTRACT: Much of our knowledge of how reward information is processed in the brain comes from a rich animal literature. Recently, the advancement of neuroimaging techniques has allowed researchers to extend such investigations to the human brain. A common finding across species and methodologies is the involvement of the striatum, the input structure of the basal ganglia, in a circuit responsible for mediating goal-directed behavior. Central to this idea is the role of the striatum in the processing of affective stimuli, such as rewards and punishments. The goal of this article is to probe the human reward circuit, specifically the striatum and its subdivisions, with an emphasis on how the affective properties of outcomes or feedback influence the underlying neural activity and subsequent decision making. Discussion will first focus on anatomical and functional considerations regarding the striatum that have emerged from animal models. The rest of the article will center on how human neuroimaging studies map to findings from the animal literature, and how more recently, this research can be extended into the social and economic domains.

KEYWORDS: reward; punishment; striatum; incentive; valence; neuroeconomics; instrumental conditioning; goal-directed behavior; caudate nucleus; nucleus accumbens; dopamine

INTRODUCTION

Rewards can broadly be defined as desirable outcomes that serve to influence behavior. Information conveyed by rewards is important for learning about and deciding between different courses of action. As our behavior is motivated by the outcomes of our actions, day-to-day activities, such as going to work, are performed routinely to either achieve a reward (e.g., receiving a paycheck) or to avoid a punishment (e.g., losing your job). Thus, rewards have been posited to serve various functions, such as inducing subjective feelings of pleasure, eliciting exploratory or approach behavior, and increasing the frequency and

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intensity of behaviors that lead to rewards.¹ Central to understanding how rewards impact goal-directed behavior is an appreciation of how rewards affect typical neural processes, which in turn lead to changes in behavior. Therefore, a necessary step in understanding behavior is to understand how knowledge of rewards and punishments is represented in our brain, and how such knowledge leads to learning of new associations that serve to guide goal-directed behavior (e.g., going to work leads to monetary income).

The goal of this article is to survey the current literature on the neural correlates of reward-related processing, with an emphasis on how the affective properties of outcomes or feedback influence choice behavior and, consequently, goal-directed behavior. One brain structure in particular, the striatum, has been thought to be involved in reward-related processes. The striatum is the recipient of cortical and dopaminergic projections, being centrally positioned in functional loops that exert an influence over motor and cognitive aspects of behavior.²⁻⁴ Thus, the focus of the discussion will be on the contributions of the human striatum to reward-related processing.

The first section of this article involves a brief review of basal ganglia anatomy and function, including support from studies in rodents and non-human primates, which highlight anatomical and functional divisions within the striatum. The second section outlines early efforts aimed at characterizing the response of the human striatum to simple behaviors and reward outcomes. Based on current neuroimaging data, the third section then considers the potential role of the human striatum and its specific subdivisions in reward-related processing. The fourth section looks at how the striatum signal can be modulated by properties of reward (e.g., probability of consumption), followed by a discussion in the fifth section of how such signals in the striatum are influenced by more complex social interactions that occur during day-to-day behavior (e.g., trust). Finally, the last section briefly describes some outstanding questions in the field and possible extensions of this work.

THE STRIATUM: ANATOMICAL AND FUNCTIONAL CONSIDERATIONS

The basal ganglia complex is formed by a group of structures that exert various functions primarily related to motor and learning aspects of behavior. The main structures that form the basal ganglia are the striatum, the globus pallidus, the subthalamic nucleus, and the substantia nigra. The globus pallidus and substantia nigra can further be subdivided into smaller components, and most of these subsections, working in conjunction with the glutamatergic projections from the subthalamic nucleus, serve as output structures of the basal ganglia.⁵ A specific portion of the substantia nigra (the pars compacta division) produces dopamine (DA), a neurotransmitter found to innervate areas

of the basal ganglia complex, such as the striatum, that is involved in motor and reward processes.⁶

The main input unit of the basal ganglia is the striatum, which receives synaptic input from cortical and subcortical afferents, such as motor cortical input and dopaminergic projections from substantia nigra (but also other midbrain nuclei, such as the ventral tegmental area^{2,4,5,7-9}). The striatum can be further subdivided into dorsal and ventral components. The dorsal striatum primarily consists of the caudate nucleus, an extensive structure that lies medially in the brain (adjacent to the lateral ventricles) and the putamen, which expands ventrally and laterally to the caudate nucleus. The dorsal striatum receives extensive projections from dorsolateral prefrontal cortex, as well as other surrounding frontal regions (e.g., premotor cortex, frontal eye fields^{5,8}). The ventral striatum consists primarily of the nucleus accumbens (although portions of the putamen and ventral caudate are also considered part of the ventral striatum) and receives extensive projections from ventral frontal regions (orbitofrontal, ventromedial, and ventrolateral cortex^{10,11}). As previously mentioned, both the dorsal and ventral striatum also receive dopaminergic input from substantia nigra and ventral tegmental area, respectively. In addition, the striatum (especially ventral portions) has connections with limbic areas implicated in emotional processing, such as the amygdala.¹⁰

Historically, the basal ganglia complex has been considered a collection of structures involved in motor functions. This is predominantly due to observations of motor deficits in patients afflicted with Parkinson's disease, a neurodegenerative disorder that affects the microcircuitry of the basal ganglia. More recently, however, research has shown that the multiple corticostriatal loops that connect the basal ganglia with the rest of the brain may serve different functions, ranging from the control of eye movements^{12,13} to more motivational behaviors.¹⁴⁻¹⁷ The striatum, in particular, has been linked to various aspects of learning (for review see Ref. 18), such as habit formation,¹⁹ skill learning,²⁰ and reward-related learning.^{21,22} The multifaceted striatum, therefore, has been posited to integrate information regarding cognition, motor control, and motivation. For example, Kawagoe and colleagues¹³ used a memory-guided saccade task with an asymmetric reward schedule to show that the nonhuman primate caudate nucleus is important in connecting both action (i.e., eye movements) and motivation (i.e., reward expectation) information. In this experiment, neuronal activity in the nonhuman primate caudate nucleus representing visual and memory responses was sensitive to changes in reward contingency, resulting in earlier and faster saccades during trials that led to rewards.

Within the striatum, further subdivisions (e.g., dorsal and ventral) exist that are considered to be functionally distinct. Studies in rodents have suggested that the ventral striatum, in particular the nucleus accumbens, is involved in affective and motivational processing. For instance, lesions in the rat ventral

striatum lead to deficits in approach behavior.²³ In contrast, lesions in the rat dorsal striatum lead to consummatory deficits (i.e., failure to consume a reward) or shortfalls in stimulus response learning,²⁴ suggesting a role for the dorsal striatum in more cognitive and sensorimotor functions.^{2,18,25} Although much of the existing animal research supports a functional division in the striatum between dorsal and ventral components, there are also theories that posit that a gradient of information shifts from more ventromedial (i.e., caudate and nucleus accumbens) to dorsolateral (i.e., putamen) structures during affective learning.²⁶ Irrespective of how information flows through the basal ganglia, due to its heterogeneity in terms of connectivity and functionality, the striatum finds itself in a prime position to integrate affective, motor, and cognitive information and influence goal-directed behavior.

A vast array of research implicates the striatum in reward-related processing. Neurons in the nonhuman primate striatum, for example, have been shown to respond to the anticipation^{13,27} and delivery^{12,28} of rewards. These striatal neurons have also been found to fire more vigorously for preferred rewards,²⁹ also showing modulation of activity based on different magnitudes of reward.³⁰ Further, significant increases in DA release in both dorsal and ventral striatum have been observed during cocaine self-administration in rats.^{31,32} Thus, the existing animal models suggest that presentation of affective, unpredictable outcomes contingent on a learned behavior involve the reward systems of the brain, specifically the striatum.

THE HUMAN STRIATUM AND REWARD

Recently, advances in neuroimaging methodology have allowed investigators to confirm and extend the findings of a rich animal literature. The initial efforts aimed at understanding the link between rewards and human neural responses were performed using positron emission tomography (PET). An example is a report of increased DA release in both dorsal and ventral striatum (measured by displacement of raclopride binding to D2 receptors by endogenous DA release) when participants played a video game for incentives.³³ Similar results were obtained with food rewards, as DA release has been reported to rise in the dorsal striatum of hungry participants when stimulated with food items.³⁴ Breiter and colleagues³⁵ used functional magnetic resonance imaging (fMRI) to study the human brain's reward circuit and addiction. By giving cocaine addicts injections of cocaine while in the scanner, the authors were able to show that activity in the human ventral striatum correlated to feelings of craving, while activity in the dorsal striatum correlated to feelings of the rush felt after receiving the drug. Thus, early neuroimaging experiments built on the existing animal literature by demonstrating that the human striatum is involved in reward processing, particularly when primary rewards were available for consumption (e.g., food, cocaine).

A drawback of the early PET and fMRI studies was the limitations in the experimental designs. For instance, although activation of the striatum was observed in a video game where rewards were present,³³ it is difficult to assess what the signal is due to (i.e., anticipation, delivery, or even magnitude of rewards). Thus, it was imperative for new designs to isolate specific components of the reward response. One specific paradigm was developed with the goal of probing neural responses to the delivery of monetary rewards and punishments.³⁶ In the form of a card-guessing game, participants were asked to guess if the value of a “card” was higher (values 6–9) or lower (values 1–4) than the number 5 (FIG. 1A). Following the choice, participants received the outcome of the card (the actual value) and a feedback symbol that indicated if the participant was correct (reward, monetary gain of \$1.00) or incorrect (punishment, monetary loss of \$0.50). The difference in magnitude between a positive and negative outcome is attributed to prospect theory and the idea that the impact of losses loom larger than gains.³⁷ Each trial in this event-related paradigm corresponded to one guess and one outcome, although unbeknownst to the participants, the outcomes were predetermined to ensure that each participant played the same reinforcement schedule and received the same feedback. Thus, the goal of the simple card game was to recruit the striatum with repeated presentations of unpredictable delivery of rewards and punishments.

Increases in blood oxygenation level-dependent (BOLD) responses in both dorsal and ventral striatum were observed using this paradigm, showing differential responses according to the feedback received (FIG. 1B³⁶). Specifically, at the onset of a trial, an increase in the BOLD response was observed as participants were faced with a choice and made a prediction and subsequent guess. This hemodynamic response was sustained and slowly returned to baseline when reward feedback was given, but decreased more rapidly before returning to baseline when punishment feedback was given. Replications of this paradigm were also carried out in different populations, such as adolescents³⁸ and nicotine addicts.³⁹

This was the first observation in humans of differential hemodynamic responses in the striatum to monetary outcomes of different valence (reward and punishment). Further, the findings could be mapped to the existing animal literature, supporting a role for the striatum in reward processing, and were concurrent with reports from early human imaging studies involving either rewards^{33,35,40} or delivery of positive or negative feedback.^{41–44} Other studies soon followed building on new imaging techniques and investigating different facets of the reward response. Many of these involved elegant paradigms that implicated the striatum during anticipation of both primary and secondary rewards.^{45–49}

The next step in understanding how the human striatum responded to rewards was to modulate the characterized BOLD response. An alteration to the paradigm allowed for investigation of potential changes in the striatum

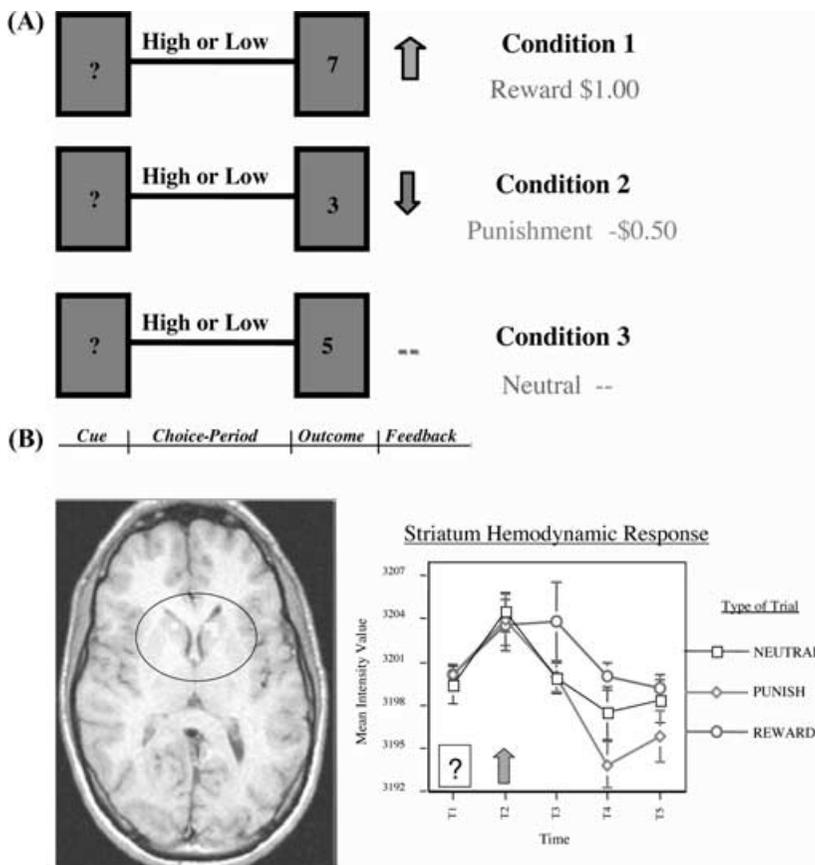


FIGURE 1. (A) The card-guessing task—a random “high or low” guess could yield one of three affective outcomes (reward, punishment, neutral). (B) Activation of both dorsal (pictured) and ventral striatum showing a differential response to reward and punishment outcomes. Time depicted as repetition time (TR) or scans, each time epoch lasting 3 sec. *Arrow* represents time of reward delivery—hemodynamic response occurs 6–9 sec after stimulus presentation. (Figure adapted from Delgado *et al.*³⁶ used with permission.)

according to variations in feedback properties, such as magnitude. The basic card-guessing game was modified to include delivery of four potential feedbacks of unpredictable valence (reward and punishment) and magnitude (large and small). While activity was once again observed in both dorsal and ventral striatum showing differential responses according to valence, magnitude differences were mostly in the dorsal striatum, where a parametric ranking of the BOLD signal according to both valence and magnitude was observed.⁵⁰ More recently, magnitude differences have been observed in the

striatum with different paradigms^{46,51,52} although the response may be context-dependent.^{53,54}

INTERPRETATION OF THE STRIATUM REWARD RESPONSE

Using event-related fMRI designs allowed researchers to characterize the response of the human striatum through different phases of reward processing. Two interesting questions surfaced, however, with respect to the striatum signal during affective outcomes. First, while activation in both dorsal and ventral striatum was observed during delivery of rewards and punishments in the card-guessing game, the intensity of the fMRI signal was higher in the dorsal striatum, predominantly the head of the caudate nucleus.³⁶ This was a slightly surprising finding—in contrast with research in animals, which often highlights the role of the ventral striatum (chiefly the nucleus accumbens) in reward processes—raising a question about the role of the human dorsal striatum. Second, what exactly did dorsal striatum activation in this paradigm mean? Were the increases in BOLD signal in the caudate nucleus due to the delivery of rewards? Or were there other features of the card-guessing paradigm (such as making a choice) that recruited the striatum?

To test these questions, a study was designed to mimic elements of the card-guessing game, while attempting to isolate the response to reward.⁵⁵ In an oddball-like paradigm, participants were presented with a series of purple squares in succession. At random intervals, an “oddball” would be presented and the participant was to press a button to indicate recognition. There were three oddballs: a reward (green upward arrow worth \$1.50), a punishment (red downward arrow worth $-\$0.75$), and a neutral oddball (a blue dash worth no monetary value). If the dorsal striatum is involved in the detection of rewards, then increases in BOLD signal in the striatum should be observed during the delivery of reward oddballs. A region of interest (ROI) analysis in the caudate nucleus defined previously, however³⁶, revealed no significant increases in BOLD response to any of the affective oddballs presented. An additional analysis found little activation in the ventral striatum as well, although the primary analysis was in the dorsal striatum and the fMRI signal in the nucleus accumbens was not optimized, thus deeming the ventral striatum results exploratory. It is worthy to note that in an oddball paradigm, the intensity of the affective stimulus is a potential issue, and a secondary reward, such as money, may not be as intense as a primary reward, such as juice, that led to activation in the ventral striatum when delivered in an unpredictable manner.⁵⁶ The goal of the study, however, was to determine what reward-related process was responsible for robustly recruiting the dorsal striatum. This experiment suggested that the caudate nucleus is not activated by the mere delivery of rewards and punishments.⁵⁵

If the caudate nucleus response in the card-guessing game is not attributed to the reward itself, then perhaps there was something about the way the reward

was attained. That is, participants had a feeling of agency, as they believed their choice or guess directly led to the reward, suggesting that perhaps learning mechanisms may be involved in this task. This hypothesis was tested in a separate study that built on the oddball paradigm.⁵⁵ Participants were once again shown a series of purple squares and were told that intermittent presentations of affective outcomes (rewards and punishments) would occur throughout. However, they were also told that they would see two anticipatory cues that predicted delivery of either a reward or a punishment. If a yellow circle was presented, participants were instructed to press one of two buttons to identify recognition of oddball. They were aware that an affective outcome followed the circle, but that the button press had no effect on the valence of the outcome. In contrast, if a blue circle was presented, participants were instructed to press one of two buttons with the perception that said button press could influence the outcome. Thus, the blue circle was much like the question mark in the card-guessing game, which elicited a button press and a prediction. In both experiments, participants felt that the reward was contingent on their behavior.

The dissociation between rewards and punishments observed previously was only replicated during presentation of the blue circle, when rewards were contingent on behavior (FIG. 2A). When participants were making a noncontingent button press (i.e., yellow circle), no differential activity was observed (FIG. 2B⁵⁵). The combined findings of both experiments in the Tricomi *et al.*⁵⁵ study suggest that the dorsal striatum, specifically the caudate nucleus, responds to the reinforcement of an action, rather than the reward per se.

Evidence from some animal studies supports a potential role for the dorsal striatum in reinforcement-based and instrumental learning.^{57,58} In a series of microdialysis studies,^{32,59} Ito and colleagues showed that dopamine levels in the dorsal striatum are elevated when rats are presented with a conditioned stimulus in which cocaine delivery is contingent upon a behavior (i.e., drug-seeking behavior), but not when a noncontingent-conditioned stimulus is presented (which leads to increases in DA release in the ventral striatum). Corroboration of these findings was also found in other neuroimaging studies using different paradigms.^{60,61} One distinct study used a conditioning paradigm incorporating fMRI and reinforcement learning models.⁶² Building on the ideas put forth by the actor-critic model,⁶³ O'Doherty and colleagues⁶² found that the ventral striatum was activated during both an instrumental and classical conditioning session, thus behaving like a "critic"; that is, it is involved in predicting potential rewards. In contrast, the dorsal striatum was activated solely during instrumental conditioning, leading the authors to posit that the dorsal striatum may be the "actor," maintaining the reward outcome of actions to optimize future choices that will lead to reward. Hence, this collection of results strongly suggest that the human dorsal striatum is involved in reward processing, specifically learning and updating actions that lead to reward, rather than representing and identifying rewards, a function postulated to occur in the frontal cortex.^{21,64,65}

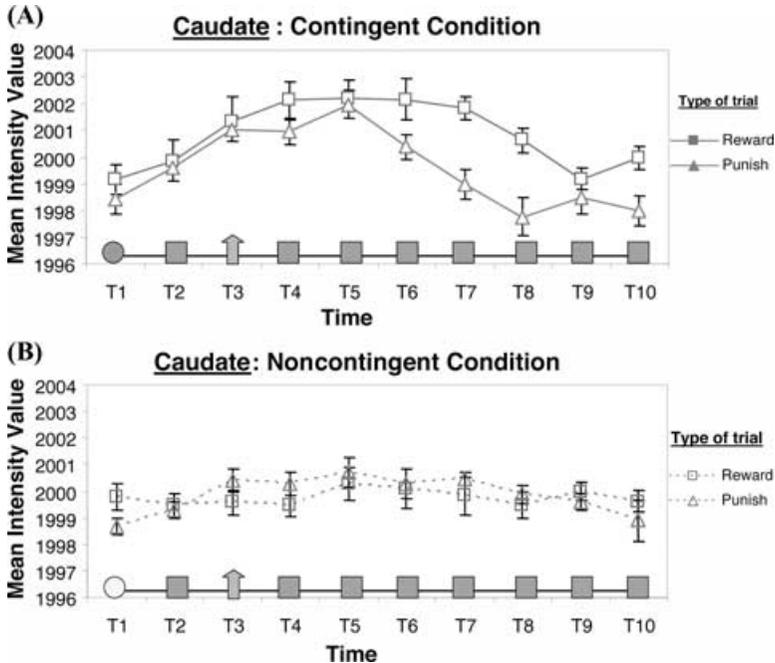


FIGURE 2. Affective oddball paradigm results. Time epochs are 1.5 sec each. Anticipatory circle, feedback arrows, and squares are depicted in both graphs. (A) Differential blood oxygenation level-dependent (BOLD) responses in the caudate nucleus to reward and punishment feedback when participants perceive a contingency between action and outcome. (B) BOLD response in the caudate nucleus during noncontingent delivery of feedback. There is no difference between the two affective conditions (reward and punishment). (Figure adapted from Tricomi *et al.*⁵⁵—reprinted from *Neuron*, with permission from Elsevier.)

THE STRIATUM AND REWARD-RELATED LEARNING

Research suggests that the human striatum is part of a circuit important during learning, being involved in evaluating current rewards to guide future actions.^{66,67} Research in patients with Parkinson's disease further suggests a link between the striatum and trial and error learning. For instance, compared with control subjects, Parkinson's patients are slower during initial learning of associative paradigms,⁶⁸ showing deficits during a feedback-based learning task, as opposed to intact learning during a nonfeedback version of the same paradigm.⁶⁹ Neuroimaging of similar cognitive learning paradigms involving feedback has resulted in activation of the striatum (mostly the dorsal striatum) differentiating between positive and negative feedback,^{43,44,70} substantiating the neuropsychological data.

The deficit in feedback-based learning in Parkinson's patients can be attributed to the low levels of DA in the striatum, as restoration of DA via agonist medication (e.g., L-dopa) also restores sensitivity to positive feedback.⁷¹ Dopamine neurons, a strong source of input into the striatum, have been associated with reward-related learning processes by neurophysiological recordings in nonhuman primates.⁷² In such studies, dopamine neurons fire first to the delivery of unpredictable rewards (e.g., juice), and second, after learning, to the earliest predictor of rewards (e.g., a light). Further, these neurons show a depression in neuronal firing when an expected reward fails to occur, suggesting a role for dopamine neurons in coding for prediction errors during affective learning. In humans, prediction errors have elicited activation in both dorsal and ventral striatum, particularly in the putamen.^{73–75}

There are parallels between the neurophysiological role of DA in learning and the increases in BOLD response observed in the striatum that were previously described in the card-guessing and affective oddball paradigms. In both experiments there was no explicit learning as participants believed the outcomes were random. Perception of control is important, however, and participants may have made predictions when a choice determined the reward. In such a scenario, the question mark or anticipatory cue may have served as the earliest predictor of a potential reward, eliciting activation at the onset of the trial. This BOLD response was then sustained if a reward was the outcome, but decreased if the choice resulted in punishment, indicating a withdrawal of an expected reward and a signal to adjust predictions or choices. The same dissociation between positive and negative feedback was observed in the caudate nucleus of participants performing a perceptual learning task.⁷⁶ Interestingly, the same participants also performed the card-guessing game in the same session, showing analogous responses between feedback received during the game and the learning task, suggesting a critical role for the caudate nucleus as a moderator of the influence of feedback on learning.

Although these feedback-based paradigms suggest a role for the dorsal striatum in reinforcement learning, the lack of explicit measures of learning does not allow such conclusion. Instead, it is necessary to measure how the reward feedback serves to shape future behavior by increasing the frequency of the optimal choice. Given the previous findings in the caudate nucleus, it can be hypothesized that during learning, caudate activation should be modulated by the perceived "value" or information provided by the reward feedback, leading to better choices for continued rewards. A modified version of the card-guessing task attempted to address this question by introducing a probabilistic cue prior to participants' guesses.²² The cue indicated the probability that the card was of high or low value, and once learned would lead to maximization of available rewards. There were three main types of cues: easy to learn (e.g., cue predicted a high card 100% of the time), harder to learn (e.g., cue predicted a high card 67% of the time), and random (e.g., cue predicted a high card 50% of the time). Overall, participants were quicker and more accurate at learning

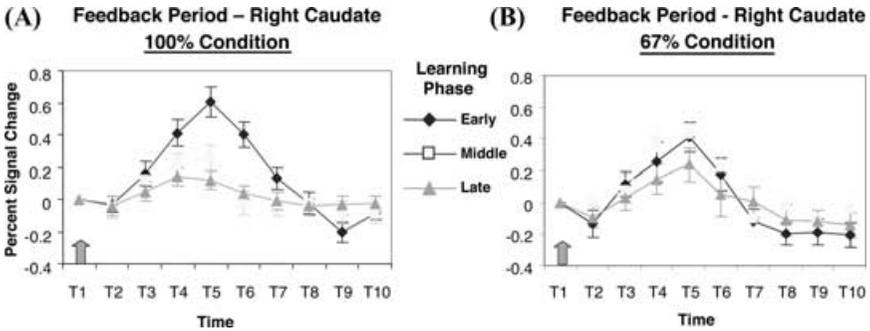


FIGURE 3. Probabilistic card-guessing task results—functional magnetic resonance imaging (fMRI) signal in caudate nucleus during delivery of positive feedback. **(A)** Activation during deterministic (100%) condition. The BOLD response to positive feedback is larger during the early trials of learning (when feedback is informative) compared to late trials (when feedback is predictable). **(B)** Activation during probabilistic condition (67%). The BOLD response to positive feedback is similar across all stages of learning, since the feedback is still informative. Each time epoch is 1.5 sec and *arrow* represents time of feedback delivery. (Figure adapted from Delgado *et al.*,²² reprinted from *NeuroImage*, with permission from Elsevier.)

the easy associations (100%). Brain imaging data suggested that the caudate nucleus was integral for performance, being activated during the initial early stages of learning (i.e., the first few trials) when feedback was most valuable. As learning progressed, however, the response in the caudate nucleus to a “reward” decreased, as the 100% cue became predictable (FIG. 3A). In contrast, more probabilistic cues (e.g., 67%) did not differ between early and late stages of learning (FIG. 3B). That is, where the reward feedback was still valuable in educating predictions, caudate activation was still observed. These data and others⁷⁷ suggest that the human caudate nucleus is an integral component of a circuit involved in learning and updating current rewards with the purpose of guiding action that will maximize reward consumption.

THE SOCIAL BRAIN: THE STRIATUM AND SOCIAL BEHAVIOR

Over the past few years, human neuroimaging studies have been successful in replicating and extending ideas put forth by animal models of reward processes. Central to these models is the role of the striatum in processing reward-related information and mediating goal-directed behavior. Yet, much of our knowledge comes from studies investigating simple rewards and behaviors. The challenge for researchers in the upcoming years is to broaden this knowledge by drawing parallels between these simple behaviors to more complex behaviors that occur in everyday human life. For instance, learning

to trust someone new is a trial and error procedure in which social interaction is crucial for developing the feeling of trust. In a thought-provoking experiment, King-Casas *et al.*⁷⁸ investigated neural responses of individuals involved in multiple rounds of economic exchange (i.e., the trust game). Participants learned through trial and error if a partner was trustworthy or not, developing trust through reciprocity. Neural signals in the dorsal striatum (the head of the caudate nucleus) mirrored the behavioral results, as the response in the caudate nucleus shifted to the earliest sign of potential “trust”—a pattern analogous to responses observed in DA models of reinforcement learning, suggesting the development of reputation.

The decision to trust can be developed through trial and error experience, but can also be influenced by previous biases or information learned through different methods. Indeed, moral beliefs can influence economic behavior and the choices we make. An individual may be willing to work for a lower salary, for example, if they believe their employer’s mission is morally praiseworthy.⁷⁹ The observation that not all learning occurs through trial and error motivated a social learning experiment involving a variation of the trust game.⁸⁰ In this interactive game, participants were instructed that they would have a choice between keeping \$1.00 or sharing the money with a partner (resulting in a \$3.00 investment). In a subsequent feedback phase, the participant then received either positive or negative feedback regarding their share decision by finding out if the partner was trustworthy (split the investment resulting in a \$1.50 reward) or untrustworthy (kept the money), respectively. Participants were also instructed they would be playing multiple rounds of this game with three fictional characters, depicted by individual bios to be of good, bad, or neutral moral character. Despite the assigned personalities, however, each partner played exactly the same. That is, each partner’s reinforcement rate was exactly 50%, suggesting that participants should learn over time to overcome their initial bias and improve their decision making.

Participants showed a degree of explicitly learning that the partners played similarly, illustrated by ratings of trustworthiness acquired during pre- and post-experimental sessions. Yet behaviorally, participants chose to share more frequently with the “good” partner, and keep more often with the “bad” partner, while no differences were observed with the “neutral” partner (FIG. 4A). This preference in choice behavior was observed both in early and late trials of the experiment, suggesting that although participants showed some explicit learning, implicitly they were still influenced by their previous bias.

As expected, the caudate nucleus was activated during the feedback phase showing differential responses to positive compared to negative feedback (FIG. 4B). This was especially true for the “neutral” partner trials, where little or no information was available to bias decisions. The “neutral” partner trials results are the most analogous to the original card-guessing task³⁶ and formation of reputation previously observed in the trust game,⁷⁸ as participants learn through trial and error how to ameliorate their decisions. When prior

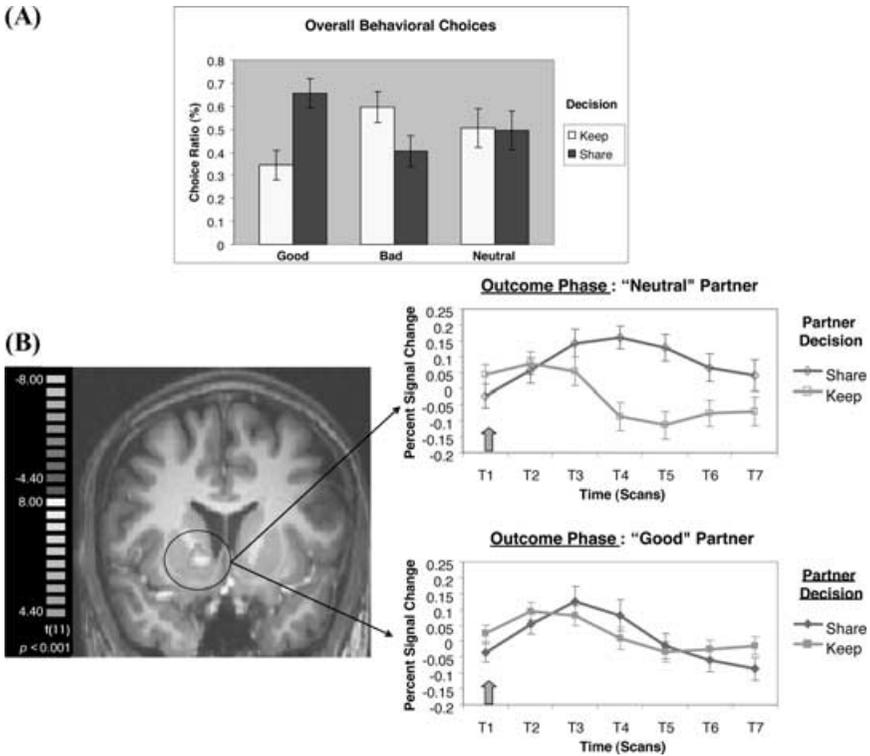


FIGURE 4. Trust game results. (A) Average choices by participants performing a multilateral trust game with three partners depicted to be of a certain moral character. (B) Activation of the ventral caudate nucleus during the outcome phase showing differential activation between positive and negative feedback during trials involving the neutral partner (where little information was available to influence decisions), but not the good partner (where previous information biased decision making). *Time epoch* represents 2 sec each and *arrow* represents time of feedback delivery. (Figure adapted from Delgado *et al.*⁸⁰)

information, such as perceived moral character, was available, however, activation in the caudate nucleus did not differentiate between positive and negative feedback.⁸⁰ There are two potential interpretations of the caudate activation. First, the strength of prior beliefs can lead participants to bypass current negative feedback thus delaying adjustments in the decision-making process, resulting in a lack of differential responses to feedback. Alternatively, the surprise that occurs when a “good” partner does not share, for example, could elicit activation in the striatum due to the saliency of the omission⁶¹ or perhaps other emotions confounded together (e.g., disbelief, regret, disappointment).

Other experiments have also investigated the role of the striatum during social and economic interactions. Many of these studies have found that the

striatum is involved during interactions that result in cooperation,⁸¹ or in response to pictures of previous cooperators,⁸² and even when exerting revenge on previous defectors.⁸³ From such experiments and the two trust experiments previously described, it is clear that the dorsal striatum, particularly the caudate nucleus, is involved in social learning. It is also apparent that prior beliefs can influence the neural mechanisms of trial and error learning, perhaps leading participants to not optimize their choice behavior.

FINAL THOUGHTS: OUTSTANDING ISSUES AND FUTURE RESEARCH

Much progress has occurred over the last few years regarding our understanding of human reward circuits. Yet, some issues and questions still remain to be resolved. First and foremost is investigating how classes of affective reinforcers differentially affect the human reward circuit. For example, are there differences in how rewards and punishments influence learning and how they are processed in the brain? Some studies suggest that while DA is involved in learning from positive feedback, it is not necessary for inferring information from negative feedback⁷¹ (e.g., punishment), which could be mediated by serotonin.⁸⁴ An extension of this question is a specific investigation of the role of the striatum in aversive processing. While this is still an open question, recent studies suggest that the human striatum is not only involved in appetitive or reward processing, but also in aversive processing,^{85,86} and even fear conditioning.⁸⁷ One possibility is that the striatum is coding for the saliency of a stimulus.⁶¹ Another possibility, however, is that the striatum is involved in affective learning, and both appetitive and aversive stimuli can motivate behavior and lead to learning.

What about differences between primary and secondary reinforcers? Due to social evolution, is money (a secondary reinforcer) as potent as a primary reinforcer (e.g., juice)? The overlap in findings between studies that use either primary or secondary reinforcers is evident, such as activation of the ventral striatum during anticipation of either type of reward.^{46,88} Nevertheless, discrepancies are also apparent, as some studies where juice rewards are used typically find activation in the ventral putamen (perhaps due to gustatory stimulation or motor properties of the tongue), while in experiments with monetary rewards, the locus of activation tends to be around the nucleus accumbens and ventral caudate. Some studies have started to directly compare primary and secondary reinforcers within subjects,⁸⁹ and although early results point to similarities in how both reinforcers affect learning, it is difficult to titrate primary and secondary reinforcers with respect to intensity, subjective value, and time of delivery (i.e., immediate vs. delayed).

A second question with respect to the human striatum's role in reward processing is its functional and anatomical hierarchy. Often in neuroimaging

studies researchers refer to activation in the striatum, without specifically parceling out the subdivisions. Even within dorsal and ventral striatum, sometimes it is unclear if the locus of activity is in the nucleus accumbens or ventral head of the caudate nucleus (see Ref. 90, for example, of human ventral striatum boundaries and DA receptor distribution). Thus, future work would enhance our knowledge about the gradient of information flow in the human striatum and how functional and anatomical subdivisions are established.

Finally, a more recent trend is to understand the social and affective human brain; that is, to investigate how social rewards modulate brain circuits involved in goal-directed behavior. There are some promising initial studies that extend findings from studies involving simple processes (e.g., reward learning) to more complex social behaviors (e.g., developing trust). In the future, investigators will also probe interactions between the human reward system in social situations and memory processes. Are there memory processes mediated by medial temporal lobe structures or prefrontal areas that, by encoding and reactivating memory traces, inhibit the striatum during trial and error learning?⁸⁰ How are prediction errors calculated during social interactions and how do they influence decision processes?

Due to anatomical considerations, the striatum is thought to be involved in possibly integrating information of reward-related information in the brain, receiving input from cortical and limbic regions that may be further modulated or shaped by mesencephalic dopaminergic projections.⁹¹ Both dorsal and ventral striatum are involved in reward processing, specifically aspects of affective learning. Although a variety of studies ranging across species suggest a link between action–outcome learning and the dorsal striatum, additional research is needed to enhance our knowledge about information flow in the striatum and potential contributions of its subdivisions to goal-directed behavior. Future investigations will also aim to extend our understanding of the human reward circuit by probing the interaction between natural rewards and punishments and social situations that occur in day-to-day interactions.

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