

A novel fMRI paradigm to dissociate the behavioral and neural components of mixed-strategy decision making from non-strategic decisions in humans

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Abstract

During competitive interactions, such as predator–prey or team sports, the outcome of one's actions is dependent on both their own choices and those of their opponents. Success in these rivalries requires that individuals choose dynamically and unpredictably, often adopting a mixed strategy. Understanding the neural basis of strategic decision making is complicated by the fact that it recruits various cognitive processes that are often shared with non-strategic forms of decision making, such as value estimation, working memory, response inhibition, response selection, and reward processes. Although researchers have explored neural activity within key brain regions during mixed-strategy games, how brain activity differs in the context of strategic interactions versus non-strategic choices is not well understood. We developed a novel behavioral paradigm to dissociate choice behavior during mixed-strategy interactions from non-strategic choices, and we used task-based functional magnetic resonance imaging (fMRI) to contrast brain activation. In a block design, participants competed in the classic mixed-strategy game, “matching pennies,” against a dynamic computer opponent designed to exploit predictability in players' response patterns. Results were contrasted with a non-strategic task that had comparable sensory input, motor output, and reward rate; thus, differences in behavior and brain activation reflect strategic processes. The mixed-strategy game was associated with activation of a distributed cortico-striatal network compared to the non-strategic task. We propose that choosing in mixed-strategy contexts requires additional cognitive demands present to a lesser degree during the control task, illustrating the strength of this design in probing function of cognitive systems beyond core sensory, motor, and reward processes.

Abbreviations: BOLD, Blood oxygen level dependent; dACC, Dorsal anterior cingulate cortex; DLPFC, Dorsolateral prefrontal cortex; EPI, Echo-planar images; FA, Flip angle; fMRI, Functional magnetic resonance imaging; FOV, Field of view; FPC, Frontopolar cortex; GLM, General linear model; IFG, Inferior frontal gyrus; IPL, Inferior parietal cortex; ITC, Inferolateral temporal cortex; MPFC, Medial prefrontal cortex; OFC, Orbitofrontal cortex; PCC, Posterior cingulate cortex; PMd, Dorsal premotor cortex; Pre-SMA, Pre-supplementary motor cortex; RFX, Random effects; RPE, Reward prediction error; SMA, Supplementary motor cortex; TE, Echo time; TMS, Transcranial magnetic stimulation; TPJ, Temporal parietal junction; TR, Repetition time; WSLs, Win–stay/lose–shift.

Douglas P. Munoz and Michael C. Dorris are senior authors contributed equally to this work.

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KEYWORDS

functional MRI, game theory, Nash equilibrium, reinforcement

1 | INTRODUCTION

Complex social interactions are a core feature of the environment in which humans live. Consider playing a game of rock–paper–scissors for \$1 a throw; each player's actions and their associated outcomes change dynamically based on their opponent's actions. On the one hand, a player should choose each of the three actions unpredictably, and with equal frequency to evade exploitation by the opponent. If both players do so, they approach the Nash equilibrium, and there is no incentive to deviate from this strategy unilaterally (Nash, 1950; Fudenberg & Tirole, 1991). On the other hand, if one's opponent departs from the Nash equilibrium, by displaying a preference for one action over another, and/or serial dependence in choice patterns, an opponent should be prepared to exploit this predictable behavior. Generally, humans and monkeys approach the Nash equilibrium during a variety of strategic games; however, systematic deviations exist, such as the win–stay/lose–shift (WLS) bias, in which individuals are more likely to repeat previously successful (rewarded) actions and switch away from previously unsuccessful (unrewarded or punished) actions (Barracough, Conroy, & Lee, 2004; Thevarajah, Mikulić, & Dorris, 2009; Vickery, Chun, & Lee, 2011). The WLS bias suggests that choices during mixed-strategy games are, in part, guided by reinforcement learning processes (Cohen & Ranganath, 2007; Hampton, Bossaerts, & O'Doherty, 2008). Understanding the dynamics of choice behavior, and the neural correlates of strategic decisions, is important as these complex interactions are ubiquitous throughout our lives, for example, during sporting competitions (Azar & Bar-Eli, 2011; Chiappori, Levitt, & Groseclose, 2002; Gauriot, Page, & Wooders, 2016) and business interactions (Thaler, 2016). Moreover, the cognitive processes involved are also putatively affected by a vast range of psychiatric and neurological disorders associated with aberrant decision-making processes, such as addictions and schizophrenia (Baek et al., 2013; Ersche et al., 2016; Kim, Lee, Sin, & Chey, 2007; Maia & Frank, 2011).

Understanding the neural basis of strategic decision making is complicated by the fact that it recruits various cognitive processes that are often shared with non-strategic forms of decision making (Griessinger & Coricelli, 2015; Lee & Seo, 2016; Ruff & Fehr, 2014), such as action selection, value estimation, working memory, response inhibition, response selection, and reward processes (Curtis & Lee, 2010; Mikulic & Dorris, 2008; Paulus, Feintein, Leland, & Simmons, 2005; Sugrue, Corrado, & Newsome, 2005; Vickery & Jiang, 2009). Fortunately, we have gained a

foundational understanding of the brain processes involved in non-strategic forms of decision making in both humans and animal models (Kable & Glimcher, 2009; Rangel, Camerer, & Montague, 2008; Wang, 2008). Additionally, the role of individual brain regions during strategic game play has been well characterized through investigations in awake behaving monkeys (Abe, Seo, & Lee, 2011; Dorris & Glimcher, 2004; Sanfey & Dorris, 2009; Seo, Barracough, & Lee, 2007; Seo, Cai, Donahue, & Lee, 2014) and in humans using event-related and model-based functional magnetic resonance imaging (fMRI) (Hampton et al., 2008; Paulus et al., 2005; Sanfey & Dorris, 2009; Vickery et al., 2011; Vickery & Jiang, 2009), and more recently, transcranial magnetic stimulation (TMS; Hill et al., 2017; Soutschek, Sauter, & Schubert, 2015). However, how coordinated activity across brain circuits differs in the context of strategic interactions relative to non-strategic forms of decision making is not well understood.

To achieve this, we develop a novel fMRI paradigm that is designed to dissociate behavioral strategies and blood oxygen level dependent (BOLD) activation during two distinct tasks: (a) an iterative version of the classic mixed-strategy game, “matching pennies” (von Neumann & Morgenstern, 1944) against a computer opponent that exploited predictability in choice patterns (Barracough et al., 2004); and (b) A non-strategic control task in which participants are required to discern the location of a colored target for a chance to obtain reward, thus engaging processes related to basic reward anticipation and outcome evaluation. Importantly, the two tasks are designed such that sensory inputs, the pattern of motor outputs, and overall reward rate are comparable. Therefore, differences between tasks should be reflective of the additional cognitive demands required during the mixed-strategy game, such as dynamically estimating the value of actions in the face of ambiguity and updating choices on the basis of past experience and reinforcement (Cohen & Ranganath, 2007; Hampton et al., 2008). First, we confirmed behaviorally that sensory input, motor outputs, and reward rate were comparable among tasks. Second, we implemented whole brain analyses contrasting activity during both tasks, allowing us to isolate key brain regions that were preferentially activated during strategic game play, above and beyond neural activity associated with choosing in non-strategic contexts.

We chose a block design, as opposed to event-related, for several reasons: (a) to capture the fast-paced, dynamic nature of repeated mixed-strategy interactions wherein one often does not have the time to prepare a response over a prolonged time period; (b) to capture the neural processes related to ongoing strategic engagement with the same opponent across

several trials (e.g., tracking a historical sequence of responses and associated outcomes); and (c) interleaving the two trial types would result in the engagement of neural processes related to task/set shifting, which were not the focus of this study and limit our ability to capture strategic processes.

2 | METHODS

Experiments were reviewed and approved by the Research and Ethics Board of Queen's University, and adhered to the principles of the Canadian Tri-Council Policy Statement on Ethical Conduct for Research Involving humans and the Declaration of Helsinki. All participants gave written informed consent prior to participation in the study.

2.1 | Participants

Twenty-five participants (11 female, mean age: 24 years \pm 3.1, range: 19–32) performed a block design experiment that contrasted behavior and BOLD activation during the strategic decision-making task (“matching pennies”) with a non-strategic decision-making task. One to four days prior to the experimental fMRI session, each participant completed an initial practice session in a sham MRI facility that was designed to mimic the scanner experience. Participants lay supine in the dark, inside an artificial MRI bore, and listened to simulated MRI noise while performing the tasks (practice session data not shown here). All participants were right-handed (assessed by the Edinburgh Handedness Inventory (Oldfield, 1971)), and all had normal or corrected-to-normal vision. Experimental data from two participants were excluded due to a high percentage of anticipatory trials during the strategic task (median reaction times were 103.70 ms and 120.74 ms). Twenty-three participants were included in the final analysis (11 female, mean age: 24 years \pm 3.29, range: 19–32).

2.2 | Experimental design and timing

Participants completed a total of 600 trials (300 non-strategic control task and 300 strategic task) consisting of two behavioral tasks that shared the same basic structure (Figure 1). Each trial was 3,200 ms in duration, and started with 800 ms of a task identification period followed by 800 ms of a centrally located fixation point. Next, two peripheral visual targets, one green and one red, appeared for 100 ms at an eccentricity of 6.5° to the left and the right of the fixation point, followed by a 700 ms response period in which the screen was blank and participants indicated their choice of target with a button press. Finally, the outcome of each trial (monetary reward) was revealed during an 800 ms period. Trials were broken into five runs of

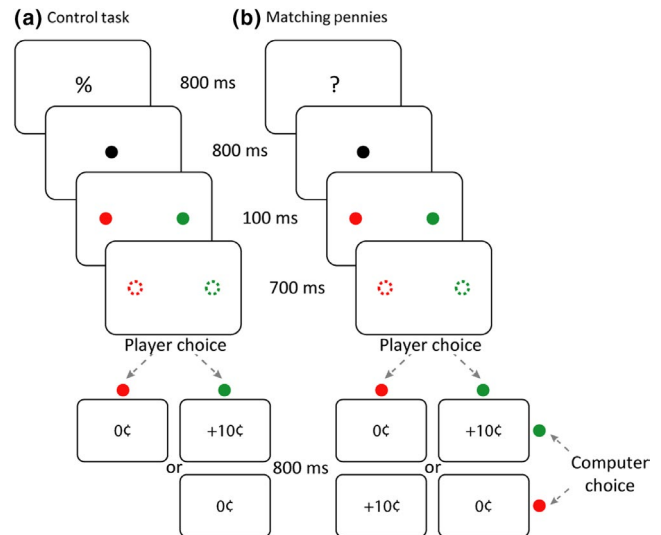


FIGURE 1 Schematic of behavioral tasks. Paradigms consisted of 50% non-strategic control trials (a), and 50% strategic trials (b). Each panel represents successive computer screens in time. Two visual targets, one red and one green, appeared on each trial, the spatial location of which was pseudorandomized, appearing on each side of the screen 50% of the time. In (a), the green target yielded \$0.10 reward on 50% of trials, and the red target yielded nothing (error trial). In (b), participants played the role of “matcher,” while the computer opponent was the “non-matcher”—if both players chose the same colored target, the participant won \$0.10; otherwise, no monetary reward was received. The outcome of each trial was revealed to the participants through either a 10¢ monetary reward (“won” trials), or a 0¢ monetary reward (“lost” trials) [Colour figure can be viewed at wileyonlinelibrary.com]

approximately 8 min in duration and consisted of 120 trials: 60 trials of the non-strategic control task (Figure 1a) and 60 trials of the strategic task (Figure 1b), in four pseudorandomly organized blocks (30 trials per block). Each block was 96 s in duration and began with a 20-s-long fixation period followed immediately by the first trial. Importantly, the location of the colored targets was pseudorandomized, appearing on each side of the screen 50% of the time during both tasks, and the spatial arrangement and timing of stimuli were identical among tasks. Participants were required to maintain fixation throughout the duration of each trial, and the final trial in each run was followed by a 20-s fixation period. Total experiment time was approximately 50 min in duration and consisted of an initial structural scan and the five functional runs.

Eye position data were recorded at 500 Hz using a Long-Range Mount SR-Research EyeLink 1,000 Eye-tracking system (SR-Research Ltd., Mississauga, Ontario, Canada; see Alahyane, Brien, Coe, Stroman, & Munoz, 2014 for details). The camera was positioned at the head of the magnet bore, and the right eye was recorded. Prior to each functional run, calibration of the eye tracker was conducted

using a five-point calibration routine. All visual stimuli were presented and behavioral responses recorded using custom MATLAB v7.9 programs (The Mathworks Inc., Natick, MA) and Psychophysics Toolbox v3 (Brainard, 1997; Pelli, 1997) running on a PC. A video projector (NEC LT265 DLP, Tokyo, Japan) was used to back-project the image onto the screen. The projector had a refresh rate of 60 Hz. Participants indicated their choices on a button response box held in both hands by pressing a leftward or rightward button with their left and right thumbs, respectively, corresponding to the location of the visual targets (Five Button Cylinder Fiber Optic Response Pad, Current Designs).

2.3 | Task procedures

2.3.1 | Non-strategic (control) task

Participants were instructed to choose the green target exclusively for the chance to receive monetary reward (Figure 1a). On 50% of the trials, the green target yielded \$0.10, and on the other 50% of the trials, it yielded nothing. Reward was administered pseudorandomly for choosing the green target, but importantly, the only strategy that could be implemented by participants to affect the outcome of this task was to select the green target exclusively. If the red target was chosen, it never yielded reward and was considered an error trial.

2.3.2 | Strategic task

Participants competed against a dynamic computer opponent in an iterative, color-based version of matching pennies (Figure 1b). Participants played the role of the “matcher,” while the computer opponent played the role of the “non-matcher”; that is, if both competitors chose the same colored target, the participant won \$0.10; otherwise, no monetary reward was received. The competitive algorithm employed by the computer opponent was based on algorithm 2 from Barraclough et al. (2004). Whereas the original opponent performed statistical analyses of the participant's historical pattern of choices (leftward/rightward target) and associated payoffs (rewarded/unrewarded) to uncover systematic biases in choice patterns (see algorithm 2 from Barraclough et al., 2004 and Lee, Conroy, McGreevy, & Barraclough, 2004 for specific details), here, we also include a statistical analysis of the historical pattern of color choices (red/green) and associated payoffs. Participants were informed of the rules and understood that they were playing a strategic game against a dynamic, competitive computer opponent. If participants approached the Nash equilibrium, and successfully evaded exploitation by the opponent, they would win on approximately 50% of trials.

During both tasks, the outcome of each trial was revealed at the end of the trial, and participants were informed of their score following each run. Importantly, compensation for participation was not fixed, and earnings were based on task performance (in the case of the control task, maximized by choosing the green target, and in the case of the mixed-strategy game, by choosing strategically and successfully evading exploitation by the computer opponent).

2.4 | MRI sequence parameters

All imaging data were acquired on a 3.0-T whole-body Siemens MRI scanner, and a 12 channel head coil. High-resolution MP-RAGE 3D T1-weighted scans were acquired for anatomical localization and coregistration (repetition time, TR = 1,760 ms, echo time, TE = 2.2 ms, flip angle, FA = 9°, field of view, FOV = 256 × 256; 176 slices, 1 mm thick). Functional images were acquired with 33 horizontal slices (3.3 mm thick) covering the brain from the top and including the frontal/prefrontal, parietal, visual areas, and basal ganglia to the level of the ventral striatum. Each functional volume consisted of T2*-weighted echo-planar images (EPI) sensitive to BOLD contrast acquired in an interleaved fashion (TR = 2000 ms, TE = 30 ms, FA = 78°, FOV = 211 × 211, matrix size 64 × 64, 3.3 mm isovoxel resolution, 244 volumes). Five functional scanning runs consisting of 244 volumes, including two discarded volumes (to compensate for T1 saturation effects), were acquired for each participant.

2.5 | Data analysis

2.5.1 | Behavioral data

Behavioral data were analyzed offline using custom MATLAB v8.1 software (The Mathworks Inc., Natick, MA). We first performed a number of behavioral analyses to determine the extent to which sensory input, reward rate, and motor output were comparable among tasks. Although we expected participants would avoid exploitation by the computer opponent by approaching the Nash Equilibrium during matching pennies (Nash, 1950), they need not do so. Therefore, we performed analyses to explore deviations from the Nash Equilibrium in participants' choice patterns.

Establishing comparability of sensory input between tasks

The pattern of sensory inputs did not differ between the tasks except for the initial “%” and “?” prompts that identified the non-strategic and strategic trial types, respectively. The two tasks were identical in terms of the timing and location of visual stimuli (Figure 1). The peripheral visual targets appeared for only 100 ms. To ensure that sensory differences did not contribute to any BOLD activation, we monitored eye

position to verify that participants foveated the fixation point and were not waiting at peripheral locations when the targets appeared or making saccades during the 100 ms target period (which would create differences in retinal inputs between tasks). We performed paired *t* tests to determine whether the number of fixation breaks during the 100 ms target presentation period differed among tasks.

Establishing comparability in reward rate between tasks

Theoretically, both tasks should yield similar reward rates of ~ 50%; in the non-strategic task, the green target yields reward pseudorandomly 50% of the time and participants had no incentive to deviate from choosing green. In the strategic task, if participants approach the Nash equilibrium (e.g., choose unpredictably; Nash, 1950), they will receive reward at a relatively random rate of ~ 50%, although biases would result in reductions in overall reward rate. We performed paired *t* tests to determine whether the number of rewarded trials differed between tasks.

Establishing comparability in motor output between tasks

We performed a number of analyses to quantify potential differences in motor output between tasks. Both tasks were designed such that participants maximized reward by allocating choices to the left and right targets with equal proportions. The location of the colored targets was pseudorandomized, appearing on each side of the screen 50% of the time during both tasks (Figure 1). During the non-strategic task, participants maximized reward by choosing the green target, which would result in allocating choices to the left and right 50% of the time. During the strategic game, choosing unpredictably—of one's own volition—with respect to target color and direction (which would result in approximately even distribution of left and right target selection) prevented exploitation by the computer opponent and, by extension, maximized reward. We performed paired *t* tests to compare how choices were allocated based on direction in the two tasks. Although comparisons across tasks of color target selection were inherently meaningless in light of the current paradigm (the optimal strategy during the control task promoted 100% allocation of choices to the green target), we also investigated the allocation of choices based on color during matching pennies using one-sample *t* tests to determine whether the proportion of green target selection differed from 50%.

Reaction time was beyond experimental control and could theoretically differ between the two tasks. In both tasks, participants were required to identify the location of the colored targets in order to respond appropriately; to choose the green target in the non-strategic task, and, based on their strategic choice, either the green or the red target in the strategic task. Therefore, we expected the reaction time distributions to be similar in both cases. To investigate this, median reaction times were compared across tasks using Wilcoxon signed-rank tests. To understand how outcome modulated response times, we

also performed exploratory analyses to investigate whether reaction times changed as a function of reward type during each task (win vs. lost trials during matching pennies, and correct vs. error trials during the control). We performed Wilcoxon signed-rank tests to ascertain whether reaction times differed as a function of reward versus non-rewarded trials in each task.

Analysis of win–stay, lose–shift strategies during matching pennies

Previous studies have shown that participants approach, but rarely achieve, the Nash equilibrium during mixed-strategy games (e.g., Vickery et al., 2011). In particular, they tend to show a win–stay, lose–shift (WSLS) bias whereby reward history dynamically affects subsequent choices (e.g., reinforcement learning). We examined the extent to which participants were using feedback to guide their choices during matching pennies by analyzing WSLS biases in both the spatial domain, and the color domain. Win–stay refers to participants tendency to select the same target as the previous trial if it was rewarded, while lose–shift refers to the tendency to switch to the alternative target following a previously unrewarded trial (Barraclough et al., 2004; Lee et al., 2004). Choices for each participants following reward or loss for each trial, *t*, was analyzed in the following way:

$$\text{win}(t) = \begin{cases} 0 & \text{for a non-response trial or loss trial} \\ 1 & \text{for a rewarded trial} \end{cases}$$

$$\text{loss}(t) = \begin{cases} 0 & \text{for a non-response trial or rewarded trial} \\ 1 & \text{for a non-rewarded trial} \end{cases}$$

Following rewarded trials ($\text{win}(t) = 1$), a win–stay event was counted for trial $t + 1$ if participants chose the same target as the previous trial (trial t) that was rewarded.

$$\text{stay}(t+1) = \begin{cases} 0 & \text{for a non-response trial or for switching to the opposite target} \\ 1 & \text{for choosing the same target following reward} \end{cases}$$

Following loss trials ($\text{loss}(t) = 1$), a lose–shift event was counted for trial $t + 1$ if participants chose the opposite target as the previous trial (trial t) where no reward was delivered.

$$\text{shift}(t+1) = \begin{cases} 0 & \text{for a non-response trial or for choosing the same target} \\ 1 & \text{for choosing the opposite target following loss} \end{cases}$$

Win–stay was calculated as:

$$P(\text{stay}|\text{win}) = \frac{\sum \text{stay}}{\sum \text{win}}$$

Lose–shift was calculated as:

$$P(\text{shift}|\text{loss}) = \frac{\sum \text{shift}}{\sum \text{loss}}$$

Win–stay, lose–shift was calculated as:

$$P(\text{WSLS}) = \frac{\sum P(\text{stay}|\text{win}) + P(\text{shift}|\text{loss})}{\sum \text{win} + \text{loss}}$$

We performed one-sample *t* tests to determine whether the probability of win–stay and/or lose–shift strategies differed from 0.5 in both the spatial domain and the color domain and also performed paired *t* tests to ascertain whether participants were more likely to use either strategy.

2.5.2 | Functional data preprocessing and analysis

All imaging data were preprocessed and analyzed using BrainVoyager QX v2.6 (Brain Innovation, Maastricht, The Netherlands). The first two imaging volumes from each run were removed to compensate for T1 saturation effects, and preprocessing steps included slice scan time correction, with cubic spline interpolation, 3D motion correction (trilinear/sinc interpolation), 3D spatial smoothing with a 4 mm FWHM Gaussian kernel, and temporal filtering (high-pass filter with cutoff of two cycles/run and linear trend removal). For each participant, data from each of the five functional runs were screened for motion artifacts exceeding 2 mm translation or 2° rotation by examining the time course movies and motion plots created with the motion correction algorithm. Seven out of 115 functional runs (limited to data within four participants) revealed head motion that exceeded 2 mm translation and were excluded from further analysis. Functional images were then coregistered to the structural image. 3-D structural images were normalized into standard Talairach space (Talairach & Tournoux, 1988) by aligning them into the AC-PC plane, followed by trilinear interpolation to warp the structural images into Talairach coordinates. These parameters were then applied to the coregistered functional data.

Our experimental conditions were modeled with boxcar predictors for the three block types used in the study: strategic task, non-strategic task, and fixation. These were convolved with BrainVoyager's 2-gamma hemodynamic response function to model the BOLD response.

2.5.3 | Whole brain analyses

To localize brain activity that was significantly higher during the strategic than the non-strategic control task, we performed group analyses with a random-effects (RFX) multi-subject general linear model (GLM) with a Z-normalization. Whole brain functional data from the non-strategic blocks was subtracted from the strategic blocks (strategic > non-strategic), and group-level statistical maps were generated at a threshold of $p < .00054$ ($t(22) = 4.98$), corrected for multiple comparisons

across the voxel population using a false discovery rate of $q = 0.005$, as well as a cluster threshold correction of 20 contiguous voxels. The cortical surface from one representative participant was reconstructed from a high-resolution anatomical image, which included segmenting the gray and white matter and inflating the boundary surface between them. This inflated cortical surface was used to overlay group statistical contrast maps for figure presentation, with the exception of the striatal activations which were superimposed on the average of the participants high-resolution 3D anatomical scans transformed into Talairach coordinate space, and constitute the *Main contrast*.

3 | RESULTS

3.1 | Behavioral results

We first performed a number of analyses to confirm that sensory, reward, and motor processes were similar across both tasks. Participants had very few non-response trials, wherein no target was chosen during the 700 ms choice period (non-strategic task group mean = 0.31%, $SD = 0.44\%$; strategic task group mean = 0.46%, $SD = 0.63\%$), and these did not differ between tasks ($t(22) = -1.01$, $p = .32$, 95% CI [-0.48, 0.17]).

3.1.1 | Sensory input

The absolute number of fixation breaks during the 100 ms target presentation period, wherein sensory differences could result from foveating the targets, were rare during both tasks (non-strategic task group mean = 0.32% of trials, $SD = 0.51\%$; strategic task group mean = 0.54% of trials, $SD = 0.89\%$) and did not differ between tasks (paired *t* test, $t(22) = 1.03$, $p = .31$).

3.1.2 | Reward rate

Reward rate did not differ between tasks (Figure 2a, non-strategic task group mean = 48.9% rewarded, $SD = 0.8\%$; strategic task group mean = 49.7% rewarded, $SD = 2.6\%$, paired-sample *t* test, $t(22) = -1.54$, $p = .14$, 95% CI [-1.80, 0.27]). During the non-strategic task, the mean error rate (trials where red was chosen instead of green) was low across participants (non-strategic task group mean = 1.9% error, $SD = 1.5\%$).

3.1.3 | Motor output

Some participants had a small, but significant rightward bias during matching pennies (Figure 2b; strategic task group mean = 54.5% right, $SD = 3.9\%$), and this was significantly higher than the non-strategic task (Figure 2b; non-strategic group mean = 49.9% right, $SD = 0.7\%$; paired-sample *t* test, $t(22) = -6.15$, $p = 3.4219e-06$, 95% CI [-6.23, -3.10]).

Participants almost always chose the green target as instructed during the non-strategic task (Figure 2c; non-strategic task group mean 98.0% green, $SD = 1.5\%$, see “Reward Rate” above), and participants displayed a small, but significant color bias during matching pennies in that the green target was chosen more often (Figure 2c; strategic task green target group mean = 51.2% green, $SD = 2.8\%$, one-sample t test, $t(22) = 2.11$, $p = .04$, $CI[50.0, 52.4]$).

Participant's reaction times were significantly shorter during the strategic task than the non-strategic task at the group level (non-strategic task group median = 319 ms, $SD = 20.86$ ms; strategic task group median = 292 ms, $SD = 44$ ms, Wilcoxon signed-rank test, $W = 242$, $Z = 3.16$, $p = .001$). Shorter reaction times could reflect the use of a spatial strategy during matching pennies, as the motor plan could be partially completed prior to target appearance (Dorris & Munoz, 1998). Primarily color-based strategies would promote reaction times similar to the non-strategic task, as additional processing time would be required to locate the selected color after its presentation. Therefore, our reaction time results suggest that some participants may have employed a spatial strategy on at least some proportion of trials. The analysis of WLSL biases that follows also suggests that participants employed both color-based and spatial-based strategies.

3.1.4 | Reaction times following win versus loss trials

During the strategic game, participants had longer reaction times following rewarded trials in comparison with lost trials (reward group median = 295.02, $SD = 44.63$, loss group median = 287.34, $SD = 45.39$, Wilcoxon rank sum test, $W = 237$, $Z = 3.01$, $p = .003$). Reaction times did not differ among trial types during the control task (reward group median = 320.36, $SD = 22.58$, error group median = 315.20, $SD = 31.74$, paired t test, Wilcoxon signed-rank test, $W = 124$, $Z = 0.29$, $p = .77$). These analyses indicate that participant's reaction times were influenced by previous experience with reward during matching pennies, with longer reaction times following rewarded trials relative to non-rewarded.

3.1.5 | Win–stay, lose–shift biases during the strategic task

A WLSL bias would provide evidence that participants were not simply responding “randomly,” but were influenced by the history of choices and outcomes during the strategic task. Participants were reliably biased toward win–stay,

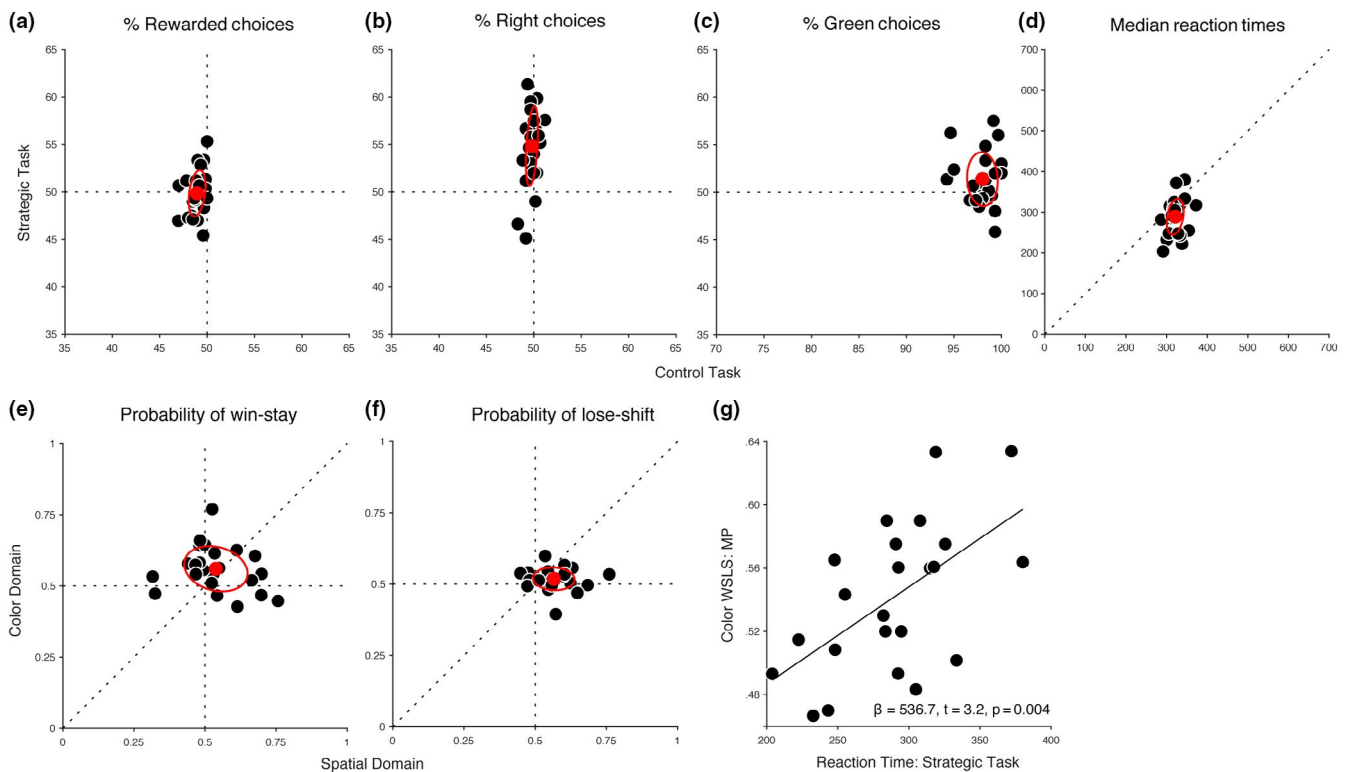


FIGURE 2 Behavior during strategic and non-strategic control tasks. Each circle represents one participant. Red filled circles and ellipses represent the mean and standard deviation across each axis, respectively. (a) Percentage of rewarded choices. (b) Percentage of rightward choices. (c) Percentage of green choices. (d) Median reaction times. (e) Probability of win–stay strategies. (f) Probability of lose–shift strategies. (g) Association between color-based win–stay, lose–shift strategies and reaction time, suggesting that those participants who emphasized color-based strategies required more time to discern the location of the colored targets prior to responding as compared to those participants who emphasized spatial-based strategies [Colour figure can be viewed at wileyonlinelibrary.com]

lose–shift strategies in both the spatial (group mean = 0.55, $SD = 0.06$, one-sample t test, $t(22) = 4.07$, $p = 5.0032e-04$, CI [0.53, 0.58]) and color (group mean = 0.54, $SD = 0.04$, one-sample t test, $t(22) = 4.09$, $p = 4.8531e-04$, CI [0.52, 0.55]) domains. Choice patterns were influenced in a multidimensional manner during the game. While the probability of win–stay strategies did not differ in the spatial domain (Figure 2e; group mean = 0.54, $SD = 0.11$) and the color domain (Figure 2e; group mean = 0.56, $SD = 0.08$, paired-sample t test, $t(22) = -0.70$, $p = .49$, 95% CI [-0.09, 0.04]), lose–shift tendencies were more prevalent in the spatial domain (Figure 2f; group mean = 0.57, $SD = 0.07$), compared to the color domain (Figure 2f; group mean = 0.52, $SD = 0.04$, paired-sample t test, $t(22) = 2.44$, $p = .02$, 95% CI [0.01, 0.08]). That we found evidence for WLS in both color and spatial domains suggests that participants were tracking both factors during the decision-making process. Moreover, we found a significant positive correlation between the probability of color-based WLS strategies and reaction time (Figure 2g; $\beta = 536.66$, $SE = 167.26$, $t(21) = 3.21$, $p = .004$), suggesting that those participants who emphasized color-based strategies required more time to discern the location of the colored targets prior to responding. Taken together, the observation of such WLS biases, in addition to the aforementioned modulation of reaction times as a function of different outcomes (win vs. loss trials), indicates that participants adjusted their behavior based, in part, on reinforcement history.

Save for a small rightward bias in few participants (Figure 2b), and the inconsistent absolute difference in reaction times (Figure 2d), results from these analyses indicate that the two tasks were largely counterbalanced in terms of sensory input, reward rate, and motor output. Importantly, systematic biases in participant's choice patterns (Figure 2e–g) suggested that participants were using feedback to guide future choice during the strategic task. Thus, our experimental design and analyses confirmed that the behavior and BOLD activation captured during matching pennies likely reflects the increased cognitive demands that differed between the two tasks.

3.2 | Neuroimaging results

Having established the compatibility of sensory, reward, and motor processing between the two tasks (Figures 1 & 2), the GLM *Main contrast* localized brain regions whose activation largely reflected strategic brain processes. Talairach coordinates of the peak significant voxel locations in all regions exceeding the statistical threshold are provided in Table 1.

Results from the GLM comparison of strategic > non-strategic tasks revealed widespread activation of a cortico-striatal network (Figure 3). Among the areas showing significantly greater activation during the strategic task were the right inferior frontal gyrus (IFG), right temporal parietal junction

(TPJ), bilateral dorsolateral prefrontal cortex (DLPFC), dorsal anterior cingulate cortex (dACC), frontopolar cortex (FPC), inferior parietal cortex (IPL), insular cortex, caudate nucleus, thalamus, as well as the pre-supplementary motor area (pre-SMA) and the supplementary motor area (SMA). The pattern of activation did not differ when these analyses were repeated using baseline corrected data (“strategic > fixation” > “control > fixation”; data not shown).

Importantly, the GLM did not reveal significantly greater activation of M1 or dorsal premotor cortex (PMd; Connolly, Goodale, Cant, & Munoz, 2007) at the group level, or in those individuals who showed a significant rightward bias during matching pennies ($n = 5$, open circles in Figure 2b), indicating that the observed pattern of BOLD activation was unlikely driven by motor differences between tasks. Further, the main GLM yielded the same pattern of activation after we removed these participants from the analyses (data not shown); thus, it is unlikely that these small absolute differences were driving the observed differences in BOLD activation.

Finally, the GLM comparison of non-strategic > strategic tasks (cold colors in Figure 3) revealed greater activation of several brain regions thought to be implicated in the default mode network (Fransson & Marrelec, 2008; Greicius, Krasnow, Reiss, & Menon, 2003), including the posterior cingulate cortex (PCC; BA 31), the left inferolateral temporal cortex (ITC), and the medial prefrontal cortex (MPFC).

Results from these analyses as well as our behavioral analyses described above revealed dissociable patterns of activation during the two tasks. Thus the activation revealed by the Main Contrast (Figure 3) is likely reflective of the increased cognitive demands involved in choosing strategically.

4 | DISCUSSION

We developed an experimental paradigm that enabled us to contrast decision-making processes during a dynamic strategic game with those involved in non-strategic contexts. Optimizing behavioral strategies during strategic game play involves flexibly choosing among several actions; the likelihood is adjusted dynamically based on experienced choices and rewards (Paulus et al., 2005; Sugrue et al., 2005). Behavioral analyses suggested that participants were strategically engaged during matching pennies, as they approached the Nash equilibrium but showed systematic deviations from this equilibrium due primarily to a WLS bias (Figure 2e–g) as reported previously (Lee et al., 2004; Vickery et al., 2011), in addition to showing differential modulation of response times as a function of outcome (wins vs. losses). Decision making in the context of mixed-strategy games involves coordination of widespread neural processes, spanning the cognitive, emotional, and limbic domains (Sanfey, 2007). Consistent with previous event-related fMRI studies (Paulus et al., 2005; Vickery et al., 2011;

Anatomical region	Talairach coordinates					Size (Voxels)
	<i>x</i>	<i>y</i>	<i>z</i>	<i>t</i>	<i>p</i>	
Strategic > non-strategic						
R dACC	6	30	25	5.23	5.60E – 05	285
L dACC	–9	28	24	5.61	1.70E – 05	256
R Frontopolar cortex (BA10)	29	52	7	7.06	1.00E – 06	379
L Frontopolar cortex (BA10)	–37	47	12	5.87	7.00E – 06	430
R Insula	32	21	4	10.15	1.90E – 09	384
L Insula	–29	19	2	7.93	1.29E – 07	397
R DLPFC	37	26	30	7.04	6.08E – 07	331
L DLPFC	–40	25	31	5.8	1.40E – 05	592
R Temporoparietal junction	55	–40	21	4.96	7.30E – 05	313
R Inferior frontal gyrus	49	15	10	6.66	2.00E – 06	251
R Inferior parietal cortex	35	–48	41	7.88	8.52E – 08	284
L Inferior parietal cortex	–38	–48	41	6.6	2.00E – 06	570
R Dorsal striatum (caudate)	12	8	9	6.21	5.00E – 06	381
L Dorsal striatum (caudate)	–13	8	7	5.17	5.40E – 05	419
R Thalamus	6	–11	5	4.96	1.43E – 04	244
L Thalamus	–7	–11	4	4.76	1.63E – 04	298
Pre-SMA	3	30	44	5.98	1.20E – 05	216
SMA	2	12	47	6.45	9.00E – 06	491
Non-strategic > strategic						
Posterior cingulate	–4	–56	20	5.36	2.50E – 05	407
L Inferolateral temporal	–53	–9	–12	5.23	4.80E – 05	717
Medial prefrontal cortex	–2	44	–6	4.51	2.18E – 04	685

Note: Abbreviations: dACC, dorsal anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; L, left; PFC, prefrontal cortex; R, right; SMA, supplementary motor area.

Vickery & Jiang, 2009) and electrophysiological findings in monkeys (Dorris & Glimcher, 2004; Seo, Barraclough, & Lee, 2009), our fMRI analyses confirmed that strategic game play recruited a cortico-striatal network in the human brain, including the inferior frontal gyrus (IFG), the temporal parietal junction (TPJ), the dorsolateral prefrontal cortex (DLPFC), dorsal anterior cingulate (dACC), frontopolar cortex (FPC), inferior parietal lobe (IPL), insular cortex, caudate nucleus, thalamus, and supplementary motor complex (Figure 3 & Table 1). We therefore propose that the our experimental design captured the enhanced and specialized cognitive demands of choosing dynamically during the strategic game, above and beyond fundamental sensory, motor, and reward processes shared with choosing in non-strategic contexts.

4.1 | Known neuronal processes

In contrast to the control task in which participants were required to discern the location of a target to obtain reward (Figure

1a), mixed-strategy action selection requires several additional cognitive and limbic processes; maintaining a history of choice patterns and associated outcomes, both one's own and those of their opponent (Abe & Lee, 2011; Seo et al., 2007), representation of reinforcement magnitudes (Knutson & Cooper, 2005; Vickery et al., 2011), outcome evaluation on the basis of both affective value (Katahira et al., 2015; Paulus et al., 2005; Sanfey, Rilling, Aronson, Nystrom, & Cohen, 2003), and reinforcement schedules (including computation of reward prediction error (RPE)) (Seo et al., 2007), ultimately culminating in the selection of a final action for execution (Mikulic & Dorris, 2008; Nachev, Wydell, O'Neill, Husain, & Kennard, 2007). These diverse, yet complementary, computations have been localized to cortico-striatal structures that are reliably engaged during sophisticated social decisions, including both dorsal and ventral subcomponents of the striatum (Rilling et al., 2002), the DLPFC (Abe & Lee, 2011; Barraclough et al., 2004; Seo et al., 2007), the TPJ (Carter, Bowling, Reeck, & Huettel, 2012; Hampton et al., 2008; Hill et al., 2017), orbitofrontal (OFC)

TABLE 1 Talairach coordinates of the peak activations identified in the Main contrast

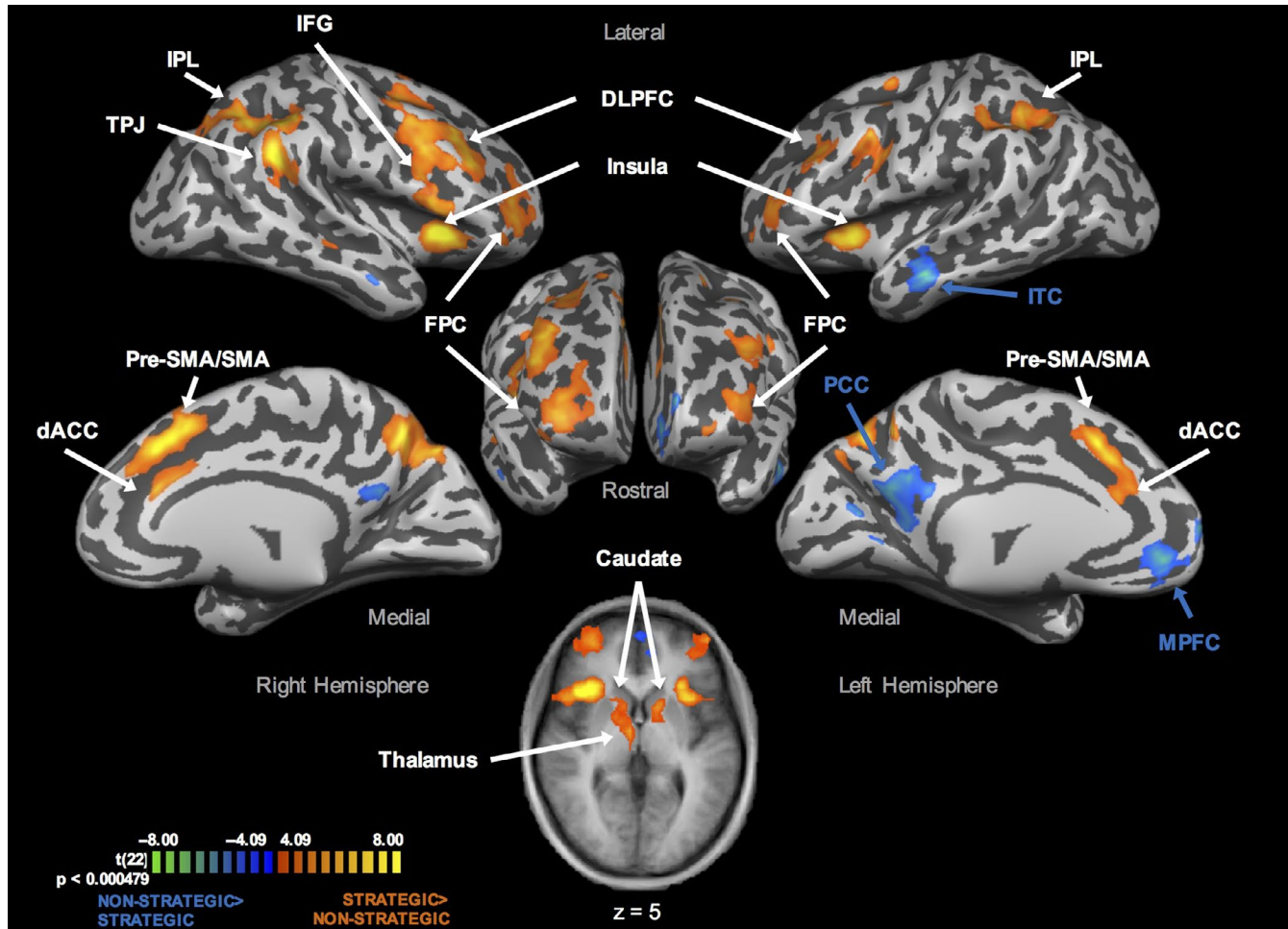


FIGURE 3 Main contrast group activation maps. Non-strategic blocks subtracted from strategic blocks (Figure 1), $p < .000537$ ($t(22) = 4.98$), corrected for multiple comparisons across the voxel population using a false discovery rate of $q = 0.005$, as well as a cluster threshold correction of 20 contiguous voxels. Significantly greater BOLD activation for the strategic task (“hot” colors), and the non-strategic task (“cold” colors), as labeled. Talairach coordinates of the peak locations in all regions exceeding the statistical threshold are provided in Table 1. IPL, inferior parietal lobule; TPJ, temporoparietal junction; IFG, inferior frontal gyrus; SMA, supplementary motor area; dACC, dorsal anterior cingulate cortex; FPC, frontopolar cortex; DLPFC, dorsolateral prefrontal cortex; ITC, inferolateral temporal cortex; PCC, posterior cingulate cortex; MPFC, medial prefrontal cortex [Colour figure can be viewed at wileyonlinelibrary.com]

(Abe & Lee, 2011; Abe et al., 2011; Vickery et al., 2011), ACC (Abe et al., 2011; Seo & Lee, 2007), parietal (Dorris & Glimcher, 2004; Paulus et al., 2005; Vickery & Jiang, 2009), and insular cortices (Paulus et al., 2005; Takahashi, Izuma, Matsumoto, Matsumoto, & Omori, 2015). The striatum, which implements reward-based action selection (Balleine, Delgado, & Hikosaka, 2007; Lau & Glimcher, 2007; O’Doherty et al., 2004; Samejima, Ueda, Doya, & Kimura, 2005; Schultz, 2002), forms strong reciprocal connections with the cerebral cortex, including many cortical regions activated in the current study (Grace, Floresco, Goto, & Lodge, 2007; Grahn, Parkinson, & Owen, 2008; Haber, Kim, Maily, & Calzavara, 2006; Selemon & Goldman-Rakic, 1988), supporting the integration of top-down inputs carrying signals necessary to incorporate information about previous choices and outcomes into the subsequent stages of decision making (Frank, 2011; Harle & Sanfey, 2012; Miller & Cohen, 2001). Greater activation of

the caudate nucleus and thalamus observed during the strategic game (Figure 3) may reflect stronger cortical input via thalamo-cortical feedback loops and integration of information across diverse cortical regions (Grahn et al., 2008; Haber et al., 2006), which were likely involved to a greater degree during the strategic task versus the control task.

4.2 | Clinical applications

Action selection requires coordination across multiple brain systems, implementing various distinct computations (Delgado, Frank, & Phelps, 2005; Lee, 2013; Rangel et al., 2008). As a result, maladaptive decision-making processes are a feature of many neurological and neuropsychiatric conditions. Deficits in reinforcement learning, cortico-striatal circuitry, and its neurotransmitter systems are increasingly being recognized as a core feature of several disorders (e.g., Parkinson’s disease and

schizophrenia; Baek et al., 2013; Ersche et al., 2016; Gradin et al., 2016; Gruner, Anticevic, Lee, & Pittenger, 2015; Kim et al., 2007; Maia & Frank, 2011), and the associated pathology within the brain often overlaps with regions found here that play a role in guiding strategic decision making. For example, cognitive and limbic processes affected by Parkinson's disease pathology overlap with those involved in mixed-strategy decision making, including reinforcement learning, working memory, and cognitive flexibility (Cools, Barker, Sahakian, & Robbins, 2001; Lewis, Slabosz, Robbins, Barker, & Owen, 2005; Moustafa, Sherman, & Frank, 2008; Slabosz et al., 2006). Further, levodopa and a class of DA agonists used to treat Parkinson's disease exacerbate cognitive symptoms, particularly in tasks requiring choosing on the basis of reinforcement history (Bódi et al., 2009; Cools et al., 2001; Frank, Seeberger, & O'Reilly, 2004; Frank, Samanta, Moustafa, & Sherman, 2007; Shohamy, Myers, Gekhman, Sage, & Gluck, 2006). An important step toward developing models of disease is to understand how pathological processes (and the treatments associated with them) differentially affect specific aspects of decision making (e.g., impairments in cognitive flexibility vs. an inability to efficiently execute motor responses). Here, we developed a paradigm with a well-designed control task representing a fundamental first step in developing a clinical tool that would allow us to disentangle how disease pathology affects specific aspects of cognition, separately from core sensory, motor, and reward deficits. However, validating the clinical efficacy of such a tool will require more detailed behavioral analyses (e.g., an investigation of trial-by-trial choice strategies), as well as a richer understanding of the role of each brain region in particular processes underlying the two tasks.

4.3 | Next steps and limitations

Although our task design provided a novel means to interrogate strategic behaviors and neural processes with relatively high specificity, the current study was not designed to probe specific cognitive roles of individual brain regions during strategic interactions. In order to capture the processes underlying more ecologically valid forms of strategic decision making (e.g., rapid decisions and engagement with an opponent across several continuous trials), we traded off the resolution to be able to disentangle particular brain processes underlying distinct computations during the mixed-strategy game. Thus, it is possible that greater activation of the network identified here was, at least in part, reflective of additional attentional processes, working memory demands, saliency and/or general cognitive control mechanisms (Menon & Uddin, 2010; Seeley et al., 2007). Indeed, the strategic task was associated with significant deactivation in areas that have been implicated in the default mode network, namely the posterior cingulate cortex (PCC), the inferolateral temporal cortex (ITC), and the medial PFC (MPFC; Figure 3), which is a consistent observation

during cognitively demanding tasks (Fransson & Marrelec, 2008; Greicius et al., 2003). Thus, although we are confident that the two tasks we employed were similar in terms of core sensory, motor, and reward processes, we cannot rule out the possibility that at least some brain activation was related to increased attentional or motivational demands. However, the task design and behavioral analyses (equal proportions of non-response trials across tasks, low percentage of error trials during the control task) suggest that the control task likely engaged basic attentional processes, albeit perhaps to a lesser extent than the matching pennies task. In the future, event-related fMRI designs will be required to carefully characterize the distinct processes underlying mixed-strategy games.

Additionally, the current study captured the *dynamic* and *interactive* behavior inherent in complex, real-world strategic engagements, albeit not the *social* components (see Delgado et al., 2005; Rilling et al., 2002; Takahashi et al., 2014; Terada & Yamada, 2017; Vickery, Kleinman, Chun, & Lee, 2015). It is possible that *social* processes inherent to real-world mixed-strategy interactions would be better assessed (albeit at the cost of experimental control) by having individuals play against a human opponent, for example, seen remotely outside of the MRI (Rilling et al., 2002), or during simultaneous fMRI recording wherein participants can interact with one another ("Hyperscanning"; Montague et al., 2002; Špiláková, Shaw, Czekóová, & Brázdil, 2019). Thus, future studies should seek to parcellate the neural processes underlying strategic interactions in real-world, social contexts.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts to declare.

AUTHOR CONTRIBUTIONS

M.C.D, B.C.C., and A.C.P. designed the experimental protocol; A.C.P. performed research and collected data; A.C.P., B.C.C., and D.P.M. analyzed data; A.C.P, B.C.C, M.C.D, and D.P.M wrote the manuscript.

DATA AVAILABILITY STATEMENT

Primary behavioral and neuroimaging data supporting the results for this manuscript can be made available upon reasonable request from the corresponding authors.

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