Decomposing the neural pathways in a simple, value-based choice

Timothy R. Koscik, Vincent Man, Andrew Jahn, Christina H. Lee, William A. Cunningham

ARTICLE INFO
Keywords:
Ventral striatum
Ventromedial prefrontal cortex
Posterior parietal cortex
fMRI
Decision
Brain-as-predictor

ABSTRACT
Understanding the neural implementation of value-based choice has been an important focus of neuroscience for several decades. Although a consensus has emerged regarding the brain regions involved, including ventromedial prefrontal cortex (vmPFC), posterior parietal cortex (PPC), and the ventral striatum (vSTR), the multifaceted nature of decision processes is one cause of persistent debate regarding organization of the value-based choice network.

In the current study, we isolate neural activity related to valuation and choice selection using a gambling task where expected gains and losses are dissociated from choice outcomes. We apply multilevel mediation analysis to formally test whether brain regions identified as part of the value-based choice network mediate between perceptions of expected value and choice to accept or decline a gamble. Our approach additionally makes predictions regarding interregional relationships to elucidate the chain of processing events within the value-based decision network. Finally, we use dynamic causal modelling (DCM) to compare plausible models of interregional relationships in value-based choice.

We observe that activity in vmPFC does not predict take/pass choices, but rather is highly associated with outcome evaluation. By contrast, both PPC and bilateral vSTR (bilaterally) mediate the relationship between expected value and choice. Interregional mediation analyses reveal that vSTR fully mediates between PPC and choice, and this is supported by DCM. Together these results suggest that vSTR, and not vmPFC nor PPC, functions as an important driver of choice.

1. Introduction

Decision neuroscience has consistently identified a set of brain regions associated with value-based choice (Bartra et al., 2013; Clithero and Rangel, 2014; Diekhof et al., 2012;Floresco, 2015; for recent reviews see Kable and Glimcher, 2009; D. J. Levy and Glimcher, 2012; Liu et al., 2011; Padoa-Schioppa, 2011; Rangel and Clithero, 2014; Rushworth et al., 2011; Sescousse et al., 2013). The value-based choice network is large and distributed, including cortical (e.g., ventromedial prefrontal (vmPFC), orbitofrontal (OFC), posterior parietal (PPC), cingulate, and insular regions) and subcortical components (e.g., ventral striatum (vSTR), amygdala). Despite general consensus on the regions involved, there are differences of opinion regarding which components are critical for choice (Hunt and Hayden, 2017; Kable and Glimcher, 2009; Padoa-Schioppa, 2011; Padoa-Schioppa and Conen, 2017; e.g., Rangel et al., 2008; Rushworth et al., 2012). There is debate regarding whether a core set of regions is necessary for all choices (e.g., Padoa-Schioppa, 2011; Padoa-Schioppa and Conen, 2017) or whether distinct systems are engaged according to choice parameters (e.g., Rangel et al., 2008; Rushworth et al., 2012). A goal of decision neuroscience is to better understand how component processes contribute and interact to generate value-based choice.

A reasonable starting point to explore neural pathways mediating choice is to begin with relatively simple choices (to simplify the space of choice parameters) and use this to focus on specific choice processes (to restrict the distribution and size of the decision-making network that is engaged). A critical question in value-based choice is which brain region (or regions) represents and integrates value-based information and forms
a choice. Given the large, distributed nature of decision-making networks in the brain, we chose to restrict our focus to regions that both encode value and predict choice from exploratory voxelwise analyses. These regions likely include relevant nodes in a network comprising the vmPFC, PPC, and vSTR. Similar value-representation and choice-selection processes have been ascribed to several regions, including the PPC, vmPFC/OFC, and vSTR (see Fig. 1). PPC activity covaries with value representation and choice response times (Basten et al., 2010; Domenech et al., 2017; Rodriguez et al., 2015). VmPFC/OFC activity represents value at decision (Boorman et al., 2009; Boorman et al., 2013; Padoa-Schioppa and Assad, 2006; Strait et al., 2014; Strait et al., 2015), integrates value information (Chib et al., 2009), and is modulated by decision duration (Rich and Wallis, 2016; Sokol-Hessner et al., 2012; Strait et al., 2014). Likewise, vSTR activity represents subjective and chosen values (Levy et al., 2010; Peters and Büchel, 2010; Strait et al., 2015) and dopamine neuromodulation of choice (for a review see Frank and Claus, 2006). These lines of research highlight the distributed nature of choice (Hunt and Hayden, 2017) but may present alternative predictions regarding the hierarchical chain of processing events in value-based choice. While some research indicates that certain decision-related regions are more proximal for choice than other regions (e.g., parietal and lateral prefrontal regions have been labelled as implementing choice process, but not valuation processes in macaques (Kable and Glimcher, 2009)), more recent views emphasize recurrence within the decision-making network along with hierarchical organization of processing timescales (Hunt and Hayden, 2017).

One reason for debate regarding the value-based choice network is that decision-making is multifaceted and requires many component processes from stimulus encoding, valuation, integration, selection, etc. In this study, we chose to isolate take/pass choices that require valuation and selection processes without adding complexity related to value comparisons when selecting between options. This simplifies choice architecture isolates component processes that are critical for value-based choice, and our aim is to trace the neural implementation of these isolated decision-making components.

To address this question we isolate decision processes from outcome evaluation and value comparison processes. To isolate decision processes, we exploit probabilistic associations between the expected values and uncertain outcomes and temporal dissociation between actions (Domenech et al., 2017; Jocham et al., 2014; Metereau and Dreher, 2015; Studer et al., 2012; e.g., Tom et al., 2007). To further isolate valuation and selection processes, we employ take/pass choices rather than more complex, multi-option choices that elicit additional comparisons between options. By isolating simple, value-based choice processes, we can explore how they are implemented in brain networks without contamination from similar, non-decision processes that may rely on similar regions. To that end, we adapted the Duplex Gamble task (Slovic and Lichtenstein, 1968) in which participants choose to take/pass a probabilistic gain and loss as a single gamble where comparator processes are not required.

We present a hierarchical mediation framework to model choices as a direct product of neural activity and environmental parameters. We formally explore whether neural activity mediates choice on a trial-by-trial basis (Bauer et al., 2006; Kenny et al., 2003) and whether trial-level activity in one region mediates the relationship between activity in other regions and choice. Together, isolation of valuation and selection processes combined with innovative analytical methods will provide novel insight into value-based choice networks within the human. Given the potential for multiple choice mediating regions (i.e., more than one region may mediate choice) and mutual mediation between regions (i.e., interregional mediation may work jointly in both directions in recurrent networks), our analyses will explore each of these possible mediation relationships.

Our approach is both hypothesis-driven, i.e., we expect PPC, vSTR, and/or vmPFC to be a critical substrate that mediates value-based choice, given the prior evidence consistent with this role, and exploratory, i.e., we were agnostic as to the precise pathway(s) and timing of information flow between these regions for choice. Moreover, we are exploring choice-mediation in a whole brain manner to explore whether other brain regions are among the critical regions for choice. Finally, despite our prediction that PPC, vSTR, and vmPFC have been implicated in the literature in decision-making, we are exploring whether these roles are restricted to decision-making or are also involved in the evaluation of choice outcomes as well.

2. Material and methods

2.1. General

We measured brain activity during a duplex gamble task using the blood-oxygenation dependent (BOLD) signal acquired with functional magnetic resonance imaging (fMRI). Given that fMRI data is inherently hierarchical (i.e., trials nested within scanning runs nested within participants), these sources of variance should be modelled with a multilevel modelling approach (e.g., Chen et al., 2013). We present the first, formal, multilevel test of the fully mediated pathway from expected value to neural activity to choice. We then extend the logic of the brain-as-predictor approach (Berkman and Falk, 2013) into a voxelwise, logistic, multilevel framework to model choices as a direct product of concurrent neural activity and environmental parameters. A key difference between our study and previous studies is the voxelwise application of generalized multilevel models data instead of regions of interest (Knutson et al., 2007). In addition, mediation analyses of neural activity (e.g., Wager et al., 2008) are useful in evaluating hypotheses relating to pathways from stimuli to brain activity to behavior as well as interregional relationships, where activity in one region may mediate between activity in other regions and behavior.

2.2. Participants

We recruited 23 individuals (14 women; one woman was excluded for being unable to complete the task, 22 individuals were analyzed in the final sample) from the Queen’s University community through advertisements. Participants provided consent in accordance with the Queen’s University Institutional Review Board. All participants had no history of neurological or psychiatric disorder, had normal or corrected vision, and were right-handed. Participants were compensated with $40.

2.3. Experimental design

Participants performed a 10-min pre-scanning task to familiarize them with the gambles to be used in the fMRI scanner. Gambles were presented as color-coded bar charts (red or blue) representing gain and loss magnitude (20, 40, 60, 80 points as bar height) and pie charts representing probabilities (13, 33, 50, 67, 83%) (Fig. 2). Gains and losses were presented simultaneously on the screen. Color and position of gambles (gains on left or right) were counterbalanced across participants.
2.5. preprocessing

TRs per run
¼ gradient echo planar pulse sequence (TE 25 ms, 0.5 mm skip) were prescribed parallel to the AC-PC line. Functional images were acquired from inferior to superior using a single-shot gradient echo planar pulse sequence (TE = 25 ms, TR = 2s, in-plane resolution = 3.5 × 3.5 mm, matrix size: 64x64, and FOV = 224 mm, TRs per run = 149).

2.6. Statistical analysis

Brain regions exhibiting activity that mediates between expected value and observed choice must meet the following criteria: (a) neural activity must be predicted by expected value, and (b) neural activity must predict choice while controlling for expected value (for a thorough discussion of mediation see Baron and Kenny, 1986). Demonstrating that neural activity is (a) predicted by expected value and (b) that neural activity predicts choice is not sufficient to demonstrate mediation, as the variance associated with each of these relationships measured separately may be completely independent. Mediation analysis quantifies the effect of one variable on the relationship between others, or in other words, mediation analysis quantifies whether the variance in (a) and (b) is associated consistent with the mediation model.

Critically, we are interested in trial-level mediation: that individuals tend to exhibit a particular response due to changes in neural activity on that trial instead of individual-level effects (e.g., membership in an experimental condition or group). By applying multilevel mediation methods, we can formally test whether neural activity mediates choices
on a trial-by-trial basis (Bauer et al., 2006; Kenny et al., 2003). Finally, once regions that mediate choice have been identified, interregional relationships can be tested, where trial-level activity in one region may mediate the relationship between activity in another region and choice. This analytic approach provides insight into process-level neural organization.

When conducting mediation analyses with fMRI data, we assume that the direction of effects is that brain activity is a product of environmental stimuli and observed choice actions result from brain activity. While it is possible for choice to cause brain activity, we assume this is less likely. When the direction of effects is less clear, such as when considering interregional relationships, mediation provides convergent evidence, but does not confirm, directionality between component processes. To explicitly test the directionality of interregional relationships, we employ dynamic causal models (DCM) to compare between hypotheses of interregional connectivity for value-based choice deemed plausible from our multilevel mediation analysis.

2.6.1. Voxelwise multilevel models

We modelled trial-related estimates of BOLD activity at each voxel in the brain in R (R Core Team, 2016) using lme4 (Bates et al., 2015) and lmerTest (Kuznetsova et al., 2015) packages as well as custom software. Core assumptions of multilevel modelling are the same as those of the general linear model (GLM); given that multilevel modelling is literally simultaneous GLM across participants and runs, processing approaches and assumptions are logically identical.

Timepoints were excluded voxelwise where the beta estimate of BOLD activity was greater than 3 standard deviations from the mean beta estimate for each subject (on average 0.15% were removed per voxel, combined across all subjects). These large spikes in the data do not reflect realistic changes in neural activity and likely result from random fluctuations in deconvolution of raw BOLD signals. Variables were mean centred as required for each model, and when necessary (i.e., for logistic models), variance components of BOLD time series estimates were decomposed into specific individual-level, subject by run-level, and trial level signals. Initial multilevel models were computed, then time points were excluded where the standardized residual of a given time point was greater than 3. Approximately 1% of data points were removed on average per model per voxel. The remaining variables were then re-mean centred and variance components were decomposed for logistic models so that outlying data points did not impact calculation of within-subjects and within-run means.

All p-values are FDR corrected (q < 0.05) using its implementation available in FSL; the cerebellum was excluded from all analyses. Reported coordinates indicate the centre of mass of a cluster in MNI space and the size of the cluster in mm³. Multilevel models included random effects of participant and scanning run. Linear multilevel models at decision predicted neural activity with expected gain and loss. Linear multilevel models at outcome predicted neural activity with gain and loss magnitude interacting with choice [coded as 1 (taken), 0 (no response), and −1 (passed)].

To model choices, we specified multilevel logistic regression models where neural activity at decision (i.e., during the time period preceding a response) predicted choice [coded 1 (taken) and 0 (passed), missed excluded] while controlling for expected gain and loss. Given our interest in trial-related changes, neural activity in choice models was decomposed into three variance components: (1) trial-related variance, beta estimate minus within-scanning run means, (2) scanning run-related variance, within-scanning run means minus within-subjects means, and (3) subject-related variance, within-subjects means minus grand mean.

2.6.2. ROI mediation in multilevel models

Potential mediating regions were identified by the conjunction of significant effects at decision: (a) expected gain related to increased activity, (b) expected loss related to decreased activity, and (c) trial-related activity predicted responses. Given this three-way conjunction and the likelihood that this resulted in small clusters, we excluded clusters (<15 voxels) to balance retention of regions likely to be involved according to prior research (e.g., PPC, vSTR, and vmPFC) and exclude extraneous small clusters and single, spurious voxels. For each region that met these criteria, we calculated the within-subjects mean time series across and then used these values to calculate the models necessary for mediation analysis.

Mediation analysis in multilevel models presents some unique challenges. For example trial-level mediation effects are nested within person-level effects (Kenny et al., 2003). One could compute separate models for each participant and then average them, but this loses the nested data structure and does not account for individual differences in mediation strength. Thus, we utilized the stacked multilevel regression procedure adapted from previous work exploring mediation analyses in multilevel models to estimate the indirect effect (Bauer et al., 2006).

Stacked regression allows simultaneous modelling of multiple multilevel models, e.g., both components of the mediated pathway (value to brain and brain to choice), which is critical for mediation analysis. Given the nested structure in multilevel data, stacked multilevel modelling accounts for the covariance of slopes in the indirect path (e.g., value to brain and brain to choice) in addition to modelling the variance in slopes for both components of the indirect path (Bauer et al., 2006). These procedures were adapted to account for the fact that some relationships require a linear fit while others (namely when predicting responses) require fitting a binomial distribution. Thus, we employed a hybrid approach and took parameter estimates from individual models that make up the indirect path: (A) trial-related changes in the mean time series predicted by overall expected value (expected gain minus expected loss), and (B) choices predicted by trial-related neural activity controlling for expected value and subject-related differences in neural activity. From these models, we constructed a covariance matrix corresponding to the covariance of models A and B. We calculated the indirect effect and covariance between A and B using a stacked regression with a linear fit. This covariance matrix is then used to calculate confidence intervals for the indirect effect using a Monte Carlo multivariate simulation (Bauer et al., 2006; Mackinnon et al., 2004). This mediation analysis procedure was repeated for each of the identified regions for expected value-choice mediation, and was repeated on pairwise groupings of regions, to explore interregional mediation of choice. In regard to interregional mediation, we chose not to explore potential multisynaptic pathways (i.e., whether a region mediates the effect between two other regions), as choice is not explicitly part of these pathways and the number of combinations quickly increases beyond reasonable computational complexity, e.g., voxelwise exploration in 2 mm³ space would require ~ 200,000 models per region pair.

2.6.3. Dynamic causal modelling of plausible value-based choice models

Together, voxelwise and interregional multilevel mediation models will isolate a set of plausible neural models of how the brain mediates value-based choice. These methods provide a powerful combination to identify and evaluate the plausible models of value-based choice across the whole brain. As mentioned above, this multilevel mediation approach is less certain when the direction of effects is unclear (as is the case for interregional mediation). By contrast, dynamic causal modelling (DCM) is impractical on a voxelwise, whole brain level, but excels when a model space is constrained to plausible models, and can more strongly infer the direction of effects. Thus, we employ behavioural DCM (SPM12 version 7219, (Penny et al., ) to provide an additional test of the likelihood of plausible interregional relationships. We constrain the model-space for DCM by including only those models where multilevel mediation is unclear in the inference of the direction of interregional effects, and exclude those that do not match mediation models of the relationship between value and choice.
3. Results

Generalized multilevel modelling revealed that expected value of gains and losses significantly predict choices [gain: $\beta = 0.117$, $z = 22.59$, $p = 5.392 \times 10^{-113}$; loss: $\beta = -0.096$, $z = -21.562$, $p = 4.046 \times 10^{-103}$]. Participants tended to take gambles when expected gain exceeded loss and pass when expected loss exceeded gain (Fig. 3).

3.1. Neural representations of value at decision and outcome

Several regions are significantly predicted by both increased activity with expected gain and decreased activity with loss value at decision, including: left PPC [Fig. 4A, ($-34$, $-78$, $28$), $260$ mm$^3$, expected gain: $\beta = 0.113$, $t(2676.3) = 3.149$, $p = 1.659 \times 10^{-5}$; expected loss: $\beta = -0.109$, $t(2675.7) = -3.06$, $p = 2.245 \times 10^{-3}$], right vSTR [Fig. 4B, $(10, 4, -8)$, $300$ mm$^3$, expected gain: $\beta = 0.119$, $t(2655.4) = 4.01$, $p = 6.142 \times 10^{-5}$; expected loss: $\beta = -0.140$, $t(2654.3) = -4.74$, $p = 2.221 \times 10^{-5}$, Fig. 4E] and the left vSTR [Fig. 4C, ($-10$, $-8$, $-110$), $220$ mm$^3$, expected gain: $\beta = 0.139$, $t(2670.0) = 3.58$, $p = 3.497 \times 10^{-4}$; expected loss: $\beta = -0.154$, $t(2666.6) = -4.00$, $p = 6.49 \times 10^{-5}$]. By contrast, a region of visual cortex [Fig. 4D, $(2, -92, 6)$, $852$ mm$^3$] increased activity to both expected gain ($\beta = 0.286$, $t(2659.6) = 5.53$, $p = 3.595 \times 10^{-8}$) and loss ($\beta = 0.179$, $t(2660.6) = 3.48$, $p = 5.015 \times 10^{-4}$) (see Fig. 4F), consistent with increased looking or attention to extreme expected value magnitude. For whole brain results at decision, including: expected value see Fig. A1.1 and Table A1, expected value magnitude see Fig. A1.2 and Table A1, expected gain see Fig. A2 and Table A2, and expected loss see Fig. A3 and Table A3.

To explore whether decision-making regions differ with regard to outcome evaluation regions, we modelled neural activity at outcome with both gain and loss values and choices. Activity in right PPC [Fig. 5A, $(38, -54, 46)$, $796$ mm$^3$] and left PPC [Fig. 5B, $(-36, -58, 44)$, $812$ mm$^3$] appears to correspond to the magnitude of outcome value, increasing activity with both gain [right PPC: $\beta = 0.244$, $t(2703.4) = 7.33$, $p = 2.979 \times 10^{-10}$; left PPC: $\beta = 0.175$, $t(2674.6) = 6.07$, $p = 1.483 \times 10^{-9}$] and loss [right PPC: $\beta = 0.125$, $t(2718.4) = 3.85$, $p = 1.192 \times 10^{-3}$; left PPC: $\beta = 0.12$, $t(2691.2) = 4.39$, $p = 1.185 \times 10^{-3}$] at outcome (Fig. 5C). By contrast activity in several regions encoded the value of received outcomes, where activity increased with received gains and decreased with received losses. These regions include right vSTR [Fig. 5D, $(12, 14, -4)$, $920$ mm$^3$, gain by choice: $\beta = 0.068$, $t(2670.4) = 3.79$, $p = 1.555 \times 10^{-4}$; loss by choice: $\beta = -0.071$, $t(2664.4) = -4.139$, $p = 3.602 \times 10^{-5}$], left vSTR [Fig. 5E, $(12, -12, -4)$, $1184$ mm$^3$, gain by choice: $\beta = 0.065$, $t(2664.7) = 3.76$, $p = 1.755 \times 10^{-5}$; loss by choice: $\beta = -0.082$, $t(2662.0) = -4.976$, $p = 6.912 \times 10^{-5}$], right vmPFC [Fig. 5F, $(6, 40, -12)$, $2508$ mm$^3$, gain by choice: $\beta = 0.093$, SE = 0.021, $t(2700.2) = 4.330$, $p = 1.548 \times 10^{-5}$; loss by choice: $\beta = -0.093$, SE = 0.020, $t(2697.4) = -4.595$, $p = 4.534 \times 10^{-5}$; see Fig. 5H], and left vmPFC [Fig. 5G, $(8, -40, -10)$, $2620$ mm$^3$, gain by choice: $\beta = 0.090$, SE = 0.023, $t(2687.8) = 3.870$, $p = 1.115 \times 10^{-4}$; loss by choice: $\beta = -0.099$, SE = 0.022, $t(2686.1) = -4.484$, $p = 7.636 \times 10^{-5}$].

For whole brain results at outcome, including: main effect of gain see Fig. A4 and Table A4, main effect of loss see Fig. A5 and Table A5, main effect of choice see Fig. A6 and Table A6, interaction between gain and choice see Fig. A7 and Table A7, interaction between loss and choice see Fig. A8 and Table A8, outcome magnitude see Fig. A9 and Table A9, outcome value see Fig. A10 and Table A10, and received value see Fig. A11 and Table A11.

Within potential, value-choice mediating regions, we calculated the indirect effect (IE) [Fig. 6A, $(12, 6, 8)$, size = 48; left vSTR, $(10, -8, 10)$, size = 48], and left PPC [Fig. 6C, $(32, -74, 28)$, size = 12] as predicted. For whole brain results where trial-related brain activity predicted choice at decision see Fig. A12 and Table A12 and for whole brain potential mediating regions see Fig. A13 and Table A13.

3.2. Identification of neural regions for mediation analysis

Potential value-choice mediating regions must (a) be predicted by expected value at decision, increased activity to expected gain and decreased activity to expected loss as demonstrated above, and (b) activity in these regions must also predict choice when controlling for expected value. We calculated voxelwise, logistic multilevel models where choice was predicted with trial-related neural activity while controlling for subject-related and scanning run-related activity and expected gain and loss. Several clusters meeting these criteria were observed: bilateral vSTR (right: $t(2718.2) = 7.978$, $p = 7.636 \times 10^{-5}$), left PPC ($t(2727.1) = 2.258$, $p = 0.025$), however, activity at decision does not predict choice for neither the left [by $-0.045$, $z = -0.501$, $p = 0.440$]. Grouping gain and loss at decision into a single, expected value predictor, expected value is represented in both left [by $-0.179$, $t(2718.2) = 2.50$, $p = 0.0124$] and right vSTR [by $-0.181$, $t(2727.1) = 2.258$, $p = 0.0240$], however, activity at decision does not predict choice for either the left [by $-0.045$, $z = -0.784$, $p = 0.490$] or the right vSTR [by $-0.029$, $z = -0.501$, $p = 0.440$]. This suggests that vSTR does not mediate choice at least in the context of the current value-based choice paradigm, indeed neither left (Indirect Effect (IE) $-0.082$, CI$_{95\%}$ = $0.345$–$0.126$) (see Fig. 7E) nor right vSTR (IE = $-0.051$, CI$_{95\%}$ = $-0.304$–$0.169$) (see Fig. 7F) mediates between value and choice.

3.3. Ventral striatum and PPC mediate between expected value and choice

Within potential, value-choice mediating regions, we calculated the mean time series of trial-related activity for each region, then modelled the neural activity in the region as a linear function of expected value (expected gain - loss), and modelled binary choice response as a logistic function of trial-related activity within each candidate region within our multilevel framework. We then used stacked multilevel modelling to estimate the covariance structure of these models simultaneously (see Methods).
4.350, \( p = \frac{1}{4} \)

\( \text{PPC: IE} \)

\( 2.728, \quad p = \frac{1}{4} \)

relationship between expected value and choice [right vSTR: IE]

Mediation analysis reveals that activity in each of these regions mediates the bilateral vSTR and left PPC meet criteria for potential mediation. Indirect effects are considered significant if the 95% confidence interval of their posterior distributions does not overlap with 0.

Given the highly correlated nature of neural activity between regions (e.g., activity in right vSTR correlates with activity in left vSTR \( r = 0.734, t(2770) = 56.87, p < 0.00 \) and left PPC \( r = 0.295, t(2770) = 16.26, p = 7.428 \times 10^{-58} \)), it is important to demonstrate that mediation is not the spurious result of common variance. To test this possibility, we explored the region within the visual cortex where activity increased in relation to expected gain and loss [but not combined expected values: \( \beta = 1.313, t(2705.8) = 1.139, p = 0.2549 \), activity predicted choice \( \beta = 0.155, z = 2.728, p = 6.35 \times 10^{-3} \), and activity was highly correlated with activity in other regions (left vSTR: \( r = 0.378, t(2770) = 21.52, p = 4.2 \times 10^{-69} \); right vSTR: \( r = 0.425, t(2770) = 24.74, p = 3.08 \times 10^{-122} \); and PPC: \( r = 0.324, t(2770) = 18.05, p = 5.68 \times 10^{-69} \)]. The indirect path through visual cortex was not significant [IE = 0.202, CI95% = -0.149–0.661] (see Fig. 7D). Thus, it is unlikely that significant mediation is due to some general, shared variance component of neural activity.

It is important to note that motor processing in the brain is necessarily proximal to the actions that implement choice relative to value processes, e.g., motor cortex directly evokes muscle movements to enact choice. Thus, motor cortex and neural substrates of value-driven behavioural control, such as the dorsal striatum (Frank and Claus, 2006) should mediate between value processes and choice. Indeed, we observed a region in left pCG (contralateral to right-handed responses) that mediates between value and choice [IE = 1.097, CI95% = 0.569–1.745], but not in dorsal striatum. While task design features allow disambiguation of processes up to abstract representations of value-based choice, action-value representations were not conditional on any feature of the gamble task. Thus, these processes could not be distinguished here.

3.4. Interregional mediation in the value-based choice network

Since multiple brain regions mediate between expected value and choice, it is important to understand how information flows between them in service of choice. We tested whether these value-choice mediators also mediate between the neural activity in other mediator regions and choice. VmpFC does not predict decision and has already been excluded as a mediator; the remaining alternatives regarding interregional mediation of choice, include the PPC and vSTR (see Fig. 8). A third alternative is that they function together to aggregate value information, where there is partial mediation for both pathways. We performed pairwise comparisons between value-choice mediators in both directions, e.g., whether right vSTR mediated between left PPC and choice and whether left PPC mediated between right vSTR and choice.
3.5. Ventral striatum mediates the relationship between PPC and choice

First, linear multilevel modelling, where brain activity in one region is used to predict activity in a potentially mediating region, reveals that all pairwise comparisons between regions are significant, which is to be expected with highly correlated brain signals. This includes: (i) left PPC activity predicted by right vSTR ($\beta = 0.475$, t(2733.0) = 28.229, p = 4.612x10^{-7}$) and left vSTR ($\beta = 0.392$, t(2731.0) = 22.287, p = 3.075x10^{-7}$); (ii) right vSTR activity predicted by left PPC ($\beta = 0.464$, t(2740.0) = 27.406, p = 2.366x10^{-7}$) and left vSTR ($\beta = 0.757$, t(2734.0) = 60.653, p = 1.751x10^{-5}$); (iii) left vSTR predicted by left PPC ($\beta = 0.417$, t(2728.0) = 23.981, p = 9.161x10^{-5}$) and right vSTR ($\beta = 0.759$, t(2730.0) = 60.877, p = 2.366x10^{-7}$). (See Fig. 9A).

Second, generalized multilevel modelling predicted choices with trial-related brain activity in the potential mediating region while controlling for activity in the other brain region and expected value (see Fig. 9B). Activity in right vSTR predicted choice consistently, after controlling for left vSTR ($\beta = 0.289$, z = 4.781, p = 1.741x10^{-5}$) or left PPC ($\beta = 0.299$, z = 6.659, p = 2.760x10^{-11}$), as did left vSTR after controlling for PPC ($\beta = 0.193$, z = 4.436, p = 9.161x10^{-5}$). (See Fig. 9C).

Finally, given the numerous pairwise comparisons, we report an FDR corrected 99.75% confidence interval corresponding to an FDR correction due to 20 tests. Pairwise mediation analysis (see Fig. 9C) indicated that both right vSTR [IE = 0.139, CI99.75% = 0.097–0.181] and left vSTR [IE = 0.080, CI99.75% = 0.044–0.117] fully mediate between activity in the PPC and choice. By contrast, this flow of information is unidirectional for choice, where PPC does not mediate between right vSTR [IE = 0.047, CI99.75% = -0.017–0.110] or left vSTR [IE = 0.047, CI99.75% = -0.003–0.100] and choice. The results are consistent with the notion that the vSTR forms a pathway through which information must flow before making a decision (see Fig. 10). We also observe that the right vSTR mediates between left vSTR and choice [IE = 0.219, CI99.75% = 0.082–0.359] but not vice versa [IE = 0.056, CI99.75% = -0.083–0.195] suggesting the vSTR mediation of decision may be somewhat lateralized in this context. To provide additional validation, we tested the mediation models using multilevel structural equation modelling as implemented in laavan for R (Rosseel, 2012). As with the stacked regression approach,
right vSTR mediated the path from expected value to choice \( z = 3.446, p = 0.001 \) and left PPC did not \( z = 0.450, p = 0.653 \). For additional interregional mediation results see Table A14, both left pCG and left lateral PPC mediate between other regions and choice, however left pCG results are likely due to motor response (button press) to implement the response. Left PPC interregional mediation indirect effects tended to be somewhat weaker than through right vSTR, i.e., right vSTR mediates between left IPCF and choice \( \beta = 0.128, CI_{99.75\%} = 0.065-0.195 \) with about twice the indirect effect of the reverse direction from left IPCF through right vSTR \( \beta = 0.072, CI_{99.75\%} = 0.025-0.137 \).

3.6. Dynamic causal modelling agrees with mediation model

To provide an additional test, whereby we can infer the directionality of interregional relationships, we used DCM to compare the plausible models of the value-based choice network. By combining multilevel mediation analysis with DCM, we can effectively reduce the model set to only those models that are plausible and consistent with the prior knowledge generated by multilevel mediation. DCM excels in indicating which models are relatively more plausible (Daunizeau et al., 2011), especially when we can constrain the model set included in the comparison (Stephan et al., 2009) by including only those models that are plausible given our multilevel mediation results. For the simple, value-based choices in our experiment, we can eliminate models from the ostensibly complete set (see Fig. 1) by: 1) excluding models where vmPPC is involved at decision as activity in this region is related to outcomes not choices per se, and 2) including only models where vSTR mediates between PPC and choice (see Fig. 8). For simplicity, we included only right vSTR in DCM models, as this had the strongest mediation effect and appeared to mediate between left vSTR and choice as well. The models include all models where vSTR mediates between PPC and choice (Fig. 11), value processing occurs in both regions (except for models E and F, where vSTR receives value information secondarily from PPC only) and: A) bidirectional PPC/vSTR connections (Fig. 11A) and B) unidirectional connection from vSTR to PPC (Fig. 11B) and C) unidirectional connection from PPC to vSTR (Fig. 11C) and D) no connection between PPC and vSTR (Fig. 11D) and E) bidirectional PPC/vSTR connections (Fig. 11E), and F) unidirectional connection from PPC to vSTR (Fig. 11F).

DCM indicated that Model C (see Fig. 10) where both vSTR and PPC process value information, but this information flows unidirectionally from PPC to vSTR, and vSTR determines choice is the most likely model of value-based choice. This was consistent when using fixed effects (relative log evidence = 12.346, posterior \( p = 1 \)) or random effects \( (\phi_p = 97.2\%) \). All other models were less likely for fixed effects \( (\text{relative log evidence: } A = 11.935, B = 307, D = 0, E = 1602, F = 1333; \text{all posterior } p = 0) \) and random effects \( (\phi_p = 2.94\%, \phi_F = 0.00\%, \phi_E = 0.00\%, \phi_D = 0.00\%), \phi_B = 0.04\% \). Model C is most consistent with our multilevel mediation results as well.

4. Discussion

Understanding value-based choice requires understanding how stimulus values are manipulated by the brain to produce choice. Research in this regard has heretofore predicted neural activity from choices and/or task parameters. We provide the first direct test of how activity in reward-related brain regions mediates between expected value and choice. This mediation constitutes direct evidence that bilateral vSTR and PPC transform incoming information regarding the expected value of a decision to select whether or not to take a gamble. By contrast, vmPFC activity does not predict choice nor does it mediate between expected value and choice selection. These data are consistent with the notion that deployment of neural resources in the value-based decision network depends on choice parameters (i.e., simple, take/pass gambles); network nodes are not necessary for all types of choices. Moreover, our observation that activity in the vSTR fully mediates between activity in the PPC suggests that vSTR has a more proximal role to choice selection (i.e., our data are consistent with the notion that the vSTR and not the PPC is the final arbiter of choice for these simple value-based choices), further refining the directionality of processing in the decision network. These results are consistent with the literature that indicates that activity in the vSTR (also labelled as nucleus accumbens) generalizes to predict future choices as well. For example, when individuals made decisions whether to fund a proposed project, vSTR activity predicted choices on a trial-by-trial basis and predicted future choices (Genevsky and Knutson, 2015; Genevsky et al., 2017). Likewise, vSTR activity has been shown to be the strongest predictor of response to advertisement (Venkatraman et al., 2015).

The timeline of processing events that is consistent with our results would start with concurrent activity in PPC and vSTR, where PPC extracts numeracy/magnitude information and vSTR extracts valuation information. Numeracy/magnitude information is fed into the vSTR to be utilized for valuation and value comparison. A decision is then formed when valuation information is compared between choices in the vSTR then fed forward to motor systems to implement the choice. This is consistent with PPC activity that has been shown to be more related to the numeric magnitude of options rather than value (Kanayet et al., 2011), which is consistent with localization of numeric representations (Cohen Kadosh et al., 2011). However, this specific interpretation is limited by the current study design, as numeric magnitude and monetary value were confounded. Additionally, lateralization of effects in the PPC appears to differ as a function of decision (left only) versus outcome (bilateral). During decision, gain and loss magnitudes need to be multiplied by their probabilities which is consistent with left lateralization of PPC activity and outcome evaluation only requires addition/subtraction to running totals which may be more related to bilateral PPC activity (Chochon et al., 1999). Future research designed to explore these effects would be needed to further delineate the potential for lateralization by numeric computation in the PPC.

Adding nuance to the literature regarding the role of the vmPPC for choice (Boorman et al., 2013; e.g., Padoa-Schioppa, 2011), our results

---

**Fig. 6. Potential mediators between expected value and choice.** Right ventral striatum (A), left ventral striatum (B), and left posterior parietal cortex (C) potentially mediate between expected value and choice. The regions displayed are the result of a conjunction between regions that increased activity with gain at decision, decreased activity with loss at decision, and trial-related activity predicted choices. Colored regions on brain slices represent z-values where trial-related activity predicted choice.
indicate that vmPFC is unlikely to be necessary for the type of simple take/pass choices used in the current study. Indeed, our data are more consistent with a role for vmPFC in outcome evaluation rather than decision. This result contrasts with other results in the literature that observed that vmPFC activity related to expected loss at decision, where take/pass gambles were not paid during fMRI scanning (further dissociating decisions from outcomes) (e.g., Tom et al., 2007). These results might be clarified by further examination of the differences between paradigms, for example, our task and that of Tom et al. (2007) differ in the difficulty of calculating the probabilistic relationship between expected values and outcomes (i.e., consistent 50/50 chances are potentially easier to calculate than variable probability values in the current design). Wunderlich et al. (2009a,b) observed that vmPFC encoded the expected value of chosen options (i.e., after an action has been selected) with a task where decisions and outcomes were probabilistically and temporally dissociated, which is consistent with our results in that vmPFC contributions to choice evaluation come after decisions are made.

Fig. 7. Mediation effects between expected value and choice.

Brain regions that mediate between expected value and choice, include: right ventral striatum (A), left ventral striatum (B), and left posterior parietal cortex (C). Activity in these regions is related to expected value at decision, trial-related activity in these regions predicts choice, and the indirect effect representing the mediation pathway from expected value through each of these brain regions to choice is significantly different from zero. Despite being highly correlated with activity in mediating regions, activity in visual cortex (D) does not mediate between expected value and choice. Moreover, neither left (E) nor right (F) ventromedial prefrontal cortex mediate decision. The leftmost column of graphs represent the relationship between expected value and neural activity at decision. The central column represents trial-related activity predicting choice. Shaded regions on left and centre columns represent 95% confidence limits. The rightmost column represents histograms of the posterior distribution of indirect effects, dashed lines indicate zero or no indirect effect, solid lines indicate the lower 95% confidence limit for each distribution, and darkly shaded distributions indicate effects significantly different from zero.

Fig. 8. Value-based choice models, mediators only.

Alternatives for the value-based choice network. Mediation results indicate that ventromedial prefrontal cortex does not mediate choice. Potential remaining regions that mediate choice include posterior parietal cortex and ventral striatum. Arrows represent information flow, where each of these regions potentially mediates between value and choice. Regions and connections that have been excluded by our mediation result are depicted in light gray, dotted lines, and circles rather than arrows.
These along with other experimental design differences highlight the need for decision-making paradigms that isolate components of value-based choice, and it underscores the notion that deployment of neural resources for decision-making is highly dependent on circumstances rather than a core region (or set of regions) always necessary for choice. Moreover, isolating components of value-based choice provides a potential base for our understanding on which we can scaffold more complex decision processes to work toward an understanding of multifaceted, real-world decision-making from the ground-up. Our data do not preclude the possibility that the vmPFC/OFC is necessary or sufficient for other value-based choices, e.g., when comparing options, when options vary in abstraction (food vs. money vs. points, etc.), or when time constraints are reduced (Jocham et al., 2014), though we have demonstrated that it is not necessary under all conditions. Further research comparing these differences in experimental manipulation within-subjects may help resolve this and other issues.

Evidence of significant mediation is insufficient to determine a causal relationship, but can act to rule out models that are causally less plausible (i.e., non-significant results argue against causal mediation, though significant results do not prove causal mediation). When the causal chain of events is clearly specified, as is assumed to be the case for expected value to brain activity to choice, interpretation is straightforward. One limitation of the current multilevel mediation method is that when the causal chain is less clear, as in interregional mediation, interpretation is less clear cut and further research will be needed to confirm these directional relationships. Our multilevel mediation method effectively constrains the set of possible models to a small set of plausible models which can then be compared using dynamic causal modelling. DCM is consistent with our interregional mediation analyses, and indicates that a unidirectional flow of information from PPC to vSTR which in turn flows to choice, is the

Fig. 9. Interregional mediation.
Pairwise interregional mediation effects for all pairwise pathways between left posterior parietal cortex (PPC), right ventral striatum (vSTR), and left vSTR. ‘Causal’ neural signals are potentially mediated by ‘mediating’ neural signals: (A) mediating signals predict causal signals for all pairwise pathways. (B) Mediating signals predicted choice after controlling for causal signals for all pairwise pathways, excluding left vSTR to right vSTR. (C) Pathways where left PPC was the mediating region did not have significant indirect effects, suggesting left PPC does not mediate between activity in other regions and choice. By contrast left vSTR mediated between left PPC only and choice, but right vSTR mediat between both left PPC and left vSTR and choice suggesting that simple, value-based choices are fully mediated by right vSTR. For (A) and (B) shaded regions represent 95% confidence intervals. For (C) histograms represent posterior distributions for the indirect effects, dotted lines indicate zero or no significant effect, solid lines represent the 99.75% confidence limits (i.e., correct for multiple pairwise comparisons), and darkly shaded histograms represent significant interregional mediation effects.

Fig. 10. Observed value-based choice network model.
The convergence of our multilevel mediation models along with consistent dynamic causal modelling results, the value-based choice network, at least for the simple take/pass decisions in our task appears to be fully mediated by the ventral striatum.
Given the lack of obvious direct connections between PPC and vSTR, this pathway is likely multi-synaptic, further experiments will need to be designed that target these portion of the pathway. Finally, our results do not preclude the possibility that the vSTR is involved in evaluating all stimuli regardless of choice, or it might be inextricably linked to implementing value-based choice and active only when value-based choices are required. Future, hypothesis-driven research could leverage these multilevel mediation techniques to further elucidate the role of the vSTR in relation to value-based decision-making and illuminate its role in relation to action selection and motor output regions.

5. Conclusion

Our results show that neural activity in the VStr and PPC mediate the relationship between expected value and choice. Moreover, the VStr provides a final common path between neural representations of value and choice. In addition, we provide an application of linear and generalized multilevel modelling to functional neuroimaging to account for the hierarchically structured error inherent to functional neuroimaging, and demonstrate that mediation models can provide evidence consistent with causal interpretations of brain activation.

Funding sources

This work was supported by the National Science & Engineering Research Council (Canada) [CC 11,378 CCF 205,586 Fund 495,218, Fund 458,036].

Declaration of competing interest

The authors declare no competing financial interests.

Acknowledgements

Thank you to Hannah Nohlen, Anthony Romyn, John Tennant, and Thalia Vrantsidis for comments, and to Samantha Mowrer & Amanda Kesek who assisted in earlier stages of the project.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2020.116764.

References

Baron, R.M., Kenny, D.A., 1986. The moderator-mediator variable distinction in social psychological research: conceptual, statistical, and strategic considerations. J. Pers. Soc. Psychol. 51 (6), 1173. https://doi.org/10.1037/0022-3514.51.6.1173.

Baron, O., McGuire, J.T., Kable, J.W., 2013. The valuation system: a coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. NeuroImage 76, 412–427. https://doi.org/10.1016/j.neuroimage.2013.02.062.

Basten, U., Biele, G., Heerken, H.R., Fiebach, C.J., 2010. How the brain integrates costs and benefits during decision making. Proc. Nat. Acad. Sci. U.S.A. 107 (50), 21767–21772. https://doi.org/10.1073/pnas.0908104107.

Bates, D., Mächler, M., Bolker, B., Walker, S., 2015. Fitting linear mixed-effects models using lme4. J. Stat. Software 67 (1), 1–48. https://doi.org/10.18637/jss.v067.i01.

Bauer, D.J., Preacher, K.J., Gil, K.M., 2006. Conceptualizing and testing random indirect effects and moderated mediation in multilevel models: new procedures and recommendations. Psychol. Methods 11 (2), 142–163. https://doi.org/10.1037/0167-8663.48.2.142.

Boorman, E.D., Rushworth, M.F., Behrens, T.E., 2013. Ventromedial prefrontal and anterior cingulate cortex adopt choice and default reference frames during sequential multi-alternative choice. J. Neurosci. Offf. J. Soc. Neurosci. 33 (6), 2242–2253. https://doi.org/10.1523/JNEUROSCI.3022-12.2013.

Bartra, O., McGuire, J.T., Kable, J.W., 2013. The valuation system: a coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. NeuroImage 76, 412–427. https://doi.org/10.1016/j.neuroimage.2013.02.062.

Basten, U., Biele, G., Heerken, H.R., Fiebach, C.J., 2010. How the brain integrates costs and benefits during decision making. Proc. Nat. Acad. Sci. U.S.A. 107 (50), 21767–21772. https://doi.org/10.1073/pnas.0908104107.

Bates, D., Mächler, M., Bolker, B., Walker, S., 2015. Fitting linear mixed-effects models using lme4. J. Stat. Software 67 (1), 1–48. https://doi.org/10.18637/jss.v067.i01.

Bartra, O., McGuire, J.T., Kable, J.W., 2013. The valuation system: a coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. NeuroImage 76, 412–427. https://doi.org/10.1016/j.neuroimage.2013.02.062.

Basten, U., Biele, G., Heerken, H.R., Fiebach, C.J., 2010. How the brain integrates costs and benefits during decision making. Proc. Nat. Acad. Sci. U.S.A. 107 (50), 21767–21772. https://doi.org/10.1073/pnas.0908104107.

Bates, D., Mächler, M., Bolker, B., Walker, S., 2015. Fitting linear mixed-effects models using lme4. J. Stat. Software 67 (1), 1–48. https://doi.org/10.18637/jss.v067.i01.

Bauer, D.J., Preacher, K.J., Gil, K.M., 2006. Conceptualizing and testing random indirect effects and moderated mediation in multilevel models: new procedures and recommendations. Psychol. Methods 11 (2), 142–163. https://doi.org/10.1037/0167-8663.48.2.142.

Berkan, E.T., Falk, E.B., 2013. Beyond brain mapping: using neural measures to predict real-world outcomes. Curr. Dir. Psychol. Sci. 22 (1), 45–50. https://doi.org/10.1177/0963721412469394.

Boorman, E.D., Behrens, T.E.J., Woolrich, M.W., Rushworth, M.F.S., 2009. How green is the grass on the other side? Frontotopical cortex and the evidence in favor of alternative courses of action. Neuron 62 (5), 733–743. https://doi.org/10.1016/j.neuron.2009.05.014.

Boorman, E.D., Rushworth, M.F., Behrens, T.E., 2013. Ventromedial prefrontal and anterior cingulate cortex adopt choice and default reference frames during sequential multi-alternative choice. J. Neurosci. Offf. J. Soc. Neurosci. 33 (6), 2242–2253. https://doi.org/10.1523/JNEUROSCI.3022-12.2013.
Levy, D.J., Snell, J., Nelson, A.J., Rustichini, A., Glimcher, P.W., 2010. Neural representation of subjective value under risk and ambiguity. J. Neurophysiol. 103 (2), 1036–1047. https://doi.org/10.1152/jn.00853.2009.

Liu, X., Hairston, J., Schrier, M., Fan, J., 2011. Common and distinct networks underling reward valence and processing stages: a meta-analysis of functional neuroimaging studies. NeuroImage. Biobehavior. Rev. 35 (5), 1219–1236. https://doi.org/10.1016/j.nbd.2010.12.012.

Mackinnon, D.P., Lockwood, C.M., Williams, J., 2004. Confidence limits for the indirect effect: distribution theories and effects sampling methods. Multivariate Behav. Res. 39 (1), 99–128. https://doi.org/10.1207/s15327906mbr3901_7.

Meterena, E., Drogan, J.–C., 2015. The medial orbitofrontal cortex encodes a general unsigned value signal during anticipation of both appetitive and aversive events. Cortex. J. Devot. Stud. Neuropath. Behav. 63, 42–54. https://doi.org/10.1016/j.cortex.2016.08.012.

Mumford, J.A., Turner, B.O., Ashby, F.G., Poldrack, R.A., 2012. Deconvolving BOLD activation in event-related designs for multivoxel pattern classification analyses. NeuroImage 59 (3), 2636–2643. https://doi.org/10.1016/j.neuroimage.2011.08.002.

Nicola, S.M., 2007. The nucleus accumbens as part of a basal ganglia action selection circuit. Psychopharmacology 191 (3), 521–550. https://doi.org/10.1007/s00213-006-0510-4.

Padoa-Schioppa, C., 2011. Neurobiology of economic choice: a good-based model. Annu. Rev. Neurosci. 34, 333–359. https://doi.org/10.1146/annurev-neuro-061010-113648.

Padoa-Schioppa, C., Anad, J.A., 2006. Neurons in the orbitofrontal cortex encode economic values. Nature 441 (7090), 223–226. https://doi.org/10.1038/nature04676.

Padoa-Schioppa, C., Conen, K.E., 2017. Orbitofrontal cortex: a neural circuit for economic decisions. Neuron 96 (4), 736–754. https://doi.org/10.1016/j.neuron.2017.09.031.

Pennartz, C.M.A., Bevers, W., Groenewegen, H.J., de Groot, J., Crone, E.A., van der Heijden, S., Kiebel, S., & Nichols, T., (Eds.), (2012). Statistical parametric mapping: the analysis of functional brain images - first ed.. Retrieved from https://www.elsevier.com/books/statistical-parametric-mapping-the-analysis-of-functional-brain-images/penny/978-0-12-372566-0.

Peters, J., Büchel, C., 2010. Reward representations of subjective reward value. Behav. Brain Res. 213 (2), 135–141. https://doi.org/10.1016/j.bbr.2010.04.031.

Rangel, A., Camerer, C., Montague, P.R., 2008. A framework for studying the neurobiology of value-based decision making. Nat. Rev. Neurosci. 9 (7), 545–556. https://doi.org/10.1038/nrn2407.

Rangel, A., Cifton, J.A., 2014. Chapter 8 - the computation of stimulus values in simple choice. In: Glimcher, P.W., Fehr, E. (Eds.), Neuroeconomics, second ed., pp. 125–148. https://doi.org/10.1016/B978-0-12-800085-5.00024-1.

R Core Team, 2016. R: A Language and Environment for Statistical Computing. Retrieved from https://core-team.net/R-core-team.html.

Rich, E.L., Wallis, J.D., 2016. Decoding subjective decisions from orbitofrontal cortex. Nat. Neurosci. 19 (9), 973–980. https://doi.org/10.1038/nn.4320.

Rissman, J., Gazzaley, A., D’Esposito, M., 2004. Measuring functional connectivity during distinct stages of a cognitive task. NeuroImage 23 (2), 752–763. https://doi.org/10.1016/j.neuroimage.2004.06.035.

Rodriguez, C.A., Turner, B.M., Van Zandt, T., McClure, S.M., 2015. The neural basis of value accumulation in intertemporal choice. Eur. J. Neurosci. 42 (5), 2179–2189. https://doi.org/10.1111/j.1460-9568.2012.08076.x.

Rosseel, Y., 2012. Lavaan: an R package for structural equation modeling and more. J. Stat. Software 48 (2), 1–36. Retrieved from https://www.jstatsoft.org/v48/i02.

R Core Team, 2016. R: A Language and Environment for Statistical Computing. Retrieved from https://www.r-project.org/.

Sokol-Hessner, P., Hutcherson, C., Hare, T., Rangel, A., 2012. Decision value computation in DLPFC and VMPFC adjusts to the available decision time. Eur. J. Neurosci. 35 (7), 1054–1056. https://doi.org/10.1111/j.1460-9568.2011.07514.x.

Salgado, S., Kaplitt, M.G., 2015. The nucleus accumbens: a comprehensive review. Stereotact. Funct. Neurosurg. 93 (2), 75–93. https://doi.org/10.1159/000368279.

Sokol-Hessner, P., Caldi, X., Segura, B., Dreher, J.–C., 2013. Processing of primary and secondary rewards: a quantitative meta-analysis and review of human functional neuroimaging studies. Neurosci. Biobehav. Rev. 37 (4), 681–696. https://doi.org/10.1016/j.neubiorev.2013.02.002.

Sokol-Hessner, P., Hutcherson, C., Hare, T., Rangel, A., 2012. Decision value computation in DLPFC and VMPCF adjusts to the available decision time. Eur. J. Neurosci. 35 (7), 1065–1074. https://doi.org/10.1111/j.1460-9568.2012.08076.x.

Stephan, K.E., Penny, W.D., Daunizeau, J., Moran, R.J., Friston, K.J., 2009. Bayesian inference for non-linear dynamic modeling of neuroimages. NeuroImage 46 (4), 1004–1017. https://doi.org/10.1016/j.neuroimage.2009.03.025.

Starr, C.E., Blanchard, C.T., Hayden, B.Y., 2014. Reward value comparison via mutual inhibition in ventromedial prefrontal cortex. Neuron 82 (8), 1347–1358. https://doi.org/10.1016/j.neuron.2014.04.032.

Starr, C.E., Sleezer, B.J., Hayden, B.Y., 2015. Signatures of value comparison in ventral striatum neurons. PLoS Biol. 13 (6), e1002173. https://doi.org/10.1371/journal.pbio.1002173.

Strait, C.E., Blanchard, C.T., Hayden, B.Y., 2014. Reward value comparison via mutual inhibition in ventromedial prefrontal cortex. Neuron 82 (6), 1347–1358. https://doi.org/10.1523/JNEUROSCI.2575-09.2009.

Takakusaki, K., Habaguchi, T., Ohtinata-Sugimoto, J., Saitoh, K., Sakamoto, T., 2003. Basal ganglia efferents to the brainstem centers controlling postural muscle tone and

Takahashi, K., Bari, A., Lu, H., Cepeda, M., 2014. The role of the posterior parietal cortex in value-based choice. NeuroImage 100, 498–508. https://doi.org/10.1016/j.neuroimage.2013.01.047.

Takakusaki, K., Habaguchi, T., Ohtinata-Sugimoto, J., Saitoh, K., Sakamoto, T., 2003. Basal ganglia efferents to the brainstem centers controlling postural muscle tone and

Takakusaki, K., Habaguchi, T., Ohtinata-Sugimoto, J., Saitoh, K., Sakamoto, T., 2003. Basal ganglia efferents to the brainstem centers controlling postural muscle tone and

Takakusaki, K., Habaguchi, T., Ohtinata-Sugimoto, J., Saitoh, K., Sakamoto, T., 2003. Basal ganglia efferents to the brainstem centers controlling postural muscle tone and
locomotion: a new concept for understanding motor disorders in basal ganglia dysfunction. Neuroscience 119 (1), 293–308. https://doi.org/10.1016/S0306-4522(03)00095-2.

Takakusaki, K., Saitoh, K., Harada, H., Kashiwayanagi, M., 2004. Role of basal ganglia-brainstem pathways in the control of motor behaviors. Neurosci. Res. 50 (2), 137-151. https://doi.org/10.1016/j.neures.2004.06.015.

Tom, S.M., Fox, C.R., Trepel, C., Poldrack, R.A., 2007. The neural basis of loss aversion in decision-making under risk. Science 315 (5811), 515–518. https://doi.org/10.1126/science.1134239.

Venkatraman, V., Dimoka, A., Pavlou, P.A., Vo, K., Hampton, W., Bollinger, B., et al., 2015. Predicting advertising success beyond traditional measures: new insights from neurophysiological methods and market response modeling. JMR, J. Market. Res. 52 (4), 436–452. https://doi.org/10.1509/jmr.13.0593.

Wager, T.D., Davidson, M.L., Hughes, B.L., Lindquist, M.A., Ochsner, K.N., 2008. Prefrontal-subcortical pathways mediating successful emotion regulation. Neuron 59 (6), 1037–1050. https://doi.org/10.1016/j.neuron.2008.09.006.

Wunderlich, K., Rangel, A., O’Doherty, J.P., 2009a. Neural computations underlying action-based decision making in the human brain. Proc. Natl. Acad. Sci. U.S.A. 106 (40), 17199–17204. https://doi.org/10.1073/pnas.0901077106.

Wunderlich, K., Rangel, A., O’Doherty, J.P., 2009b. Neural computations underlying action-based decision making in the human brain. Proc. Natl. Acad. Sci. U.S.A. 106, 17199–17204.