Report

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Double dissociation of dopamine and subthalamic nucleus stimulation on effortful cost/benefit decision making

Highlights

- Patients with Parkinson's completed an effortful cost/benefit decision-making task
- Both STN DBS and DA were manipulated ON/OFF within patients
- DA and DBS affect choice and decision time in a computationally dissociable manner
- DA asymmetrically affects costs and benefits while DBS reduces decision threshold

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In brief

Pagnier et al. provide behavioral and computational evidence that dopamine medication and subthalamic nucleus stimulation have dissociable effects on effortful cost/benefit decision making in Parkinson's patients. Using a within-subject design, dopamine increases sensitivity to benefits vs. costs, while deep brain stimulation reduces the "decision threshold" in a drift diffusion model, leading to fast but inconsistent decisions.

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Double dissociation of dopamine and subthalamic nucleus stimulation on effortful cost/benefit decision making

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SUMMARY

Deep brain stimulation (DBS) and dopaminergic therapy (DA) are common interventions for Parkinson's disease (PD). Both treatments typically improve patient outcomes, and both can have adverse side effects on decision making (e.g., impulsivity).[1,2] Nevertheless, they are thought to act via different mechanisms within basal ganglia circuits.[3] Here, we developed and formally evaluated their dissociable predictions within a single cost/benefit effort-based decision-making task. In the same patients, we manipulated DA medication status and subthalamic nucleus (STN) DBS status within and across sessions. Using a series of descriptive and computational modeling analyses of participant choices and their dynamics, we confirm a double dissociation: DA medication asymmetrically altered participants' sensitivities to benefits vs. effort costs of alternative choices (boosting the sensitivity to benefits while simultaneously lowering sensitivity to costs); whereas STN DBS lowered the decision threshold of such choices. To our knowledge, this is the first study to show, using a common modeling framework, a dissociation of DA and DBS within the same participants. As such, this work offers a comprehensive account for how different mechanisms impact decision making, and how impulsive behavior (present in DA-treated patients with PD and DBS patients) may emerge from separate physiological mechanisms.

RESULTS

"Everybody wants the most they can possibly get. For the least they can possibly do" - Todd Snider. 2003. "*Easy Money.*"

Deep brain stimulation (DBS) and dopamine (DA) medication both typically improve PD motor symptoms but can in some cases exacerbate or trigger impulsive behavior.[1,2,4,5] Although these clinical side effects appear similar, impulsivity is a broad construct and theoretical models predict dissociable mechanisms for how DA and DBS manipulations affect decision making in corticostriatal circuits.[3,6–8] In the basal ganglia, DA exerts opposite effects on D1- and D2-expressing neurons, modulating the relative sensitivity to the benefits and costs of a proposed action.[7,9,10] DA manipulations can alter this balance: increasing DA may induce biased decisions that discount potential losses and/or effort costs.[4,11–14] Conversely, low-frequency oscillatory activity from the prefrontal cortex communicates with the subthalamic nucleus (STN) to increase the decision threshold, facilitating more deliberative and hence slower and less impulsive choices.[3,15–18] High-frequency STN DBS disrupts these signals, lowering the decision threshold, improving motor function, and inducing rash decisions.[19–21] Importantly, both DA and STN DBS mechanisms have been linked to the development of impulse control disorders in Parkinson's disease (PD).[2,22–24]

The widespread comorbidity and heterogeneity of neurological and psychiatric illness imposes a pernicious challenge for precision medicine: what is the best treatment for an individual if there are multiple possible mechanistic culprits that could trigger the same symptoms? Behavioral or computational biomarkers hold promise for transforming psychiatric and neurological diagnosis and treatment.[25–28] To date, however, no single task or model has dissociated the impact of STN vs. DA mechanisms within individuals. Here, our aim is to test the basic mechanisms by which STN and DA manipulations influence motivated decision making; variations of which at the extreme could drive distinct aspects of impulsivity. Though particularly relevant for PD, inferring which circuit could drive impulsive behavior is relevant for any individual exhibiting pathological behavior (as in the case of ADHD).

We assessed the hypothesized orthogonal effects of STN DBS and DA manipulations within individual subjects performing a novel effort-based decision-making task. Participants had to choose between a high-effort, high-reward option and a low-effort, low-reward option on every trial (Figure 1A). By systematically varying the effort required to receive different rewards, we

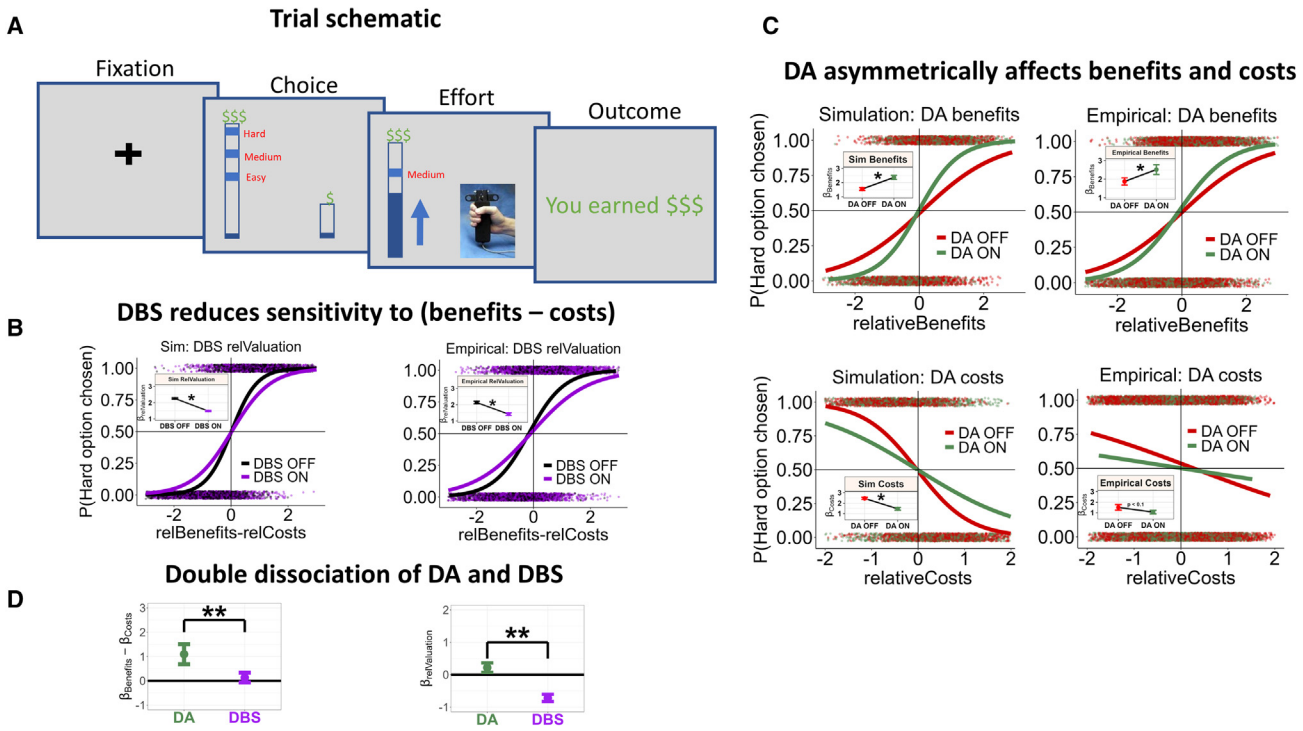

Figure 1. Experimental task design, simulations, and empirical behavior

(A) Participants chose between a hard-effort, high-reward option and a low-effort, low-reward option centered around their subject-specific indifference point (determined by an earlier titration phase). Participants then squeezed a dynamometer to fill up the selected bar. Within each DA session, participants performed the task DBS ON and DBS OFF in a pseudo-randomized order.

(B and C) Simulated and empirical effects of DBS and DA manipulations. Simulated patterns were obtained from a drift diffusion model in which evidence accumulation (drift rate) varied as a function of benefits and costs and choices were determined when this evidence reached the decision threshold (see Table S3 for DDM simulation parameters).

(B) Empirical choice patterns in model and data favor the hard-effort option with increasing net differences in benefits-costs (relValuation). Reducing decision threshold (left) predicts a shallower psychometric function with reduced sensitivity to both benefits and costs (relValuation); this pattern was observed ON vs. OFF DBS (right).

(C) Simulated and empirical data broken down into relative benefits and costs separately. DA simulations asymmetrically altered the impact of benefits vs. costs on drift rate, based on predictions from computational models of striatal opponency[7,9] in which DA elevations increase choice sensitivity to relative benefits (top) while simultaneously decreasing choice sensitivity to relative costs (bottom).[11] These patterns were observed ON vs. OFF DA (right). Insets represent individual coefficient estimates from mixed-effects models regressing DA and DBS on choice, showing mean of individual coefficients; error bars are calculated within-subject.

(D) Double dissociation of empirical coefficients extracted from mixed-effect models across subjects. DA induces within-subject differences in differential sensitivity to benefits vs. costs (left), whereas DBS lowers sensitivity to both (relValuation) (right). Error bars represent standard error.

See Table S2 for linear mixed regression outputs and Table S3 for simulation parameters.

quantified individuals' sensitivities to the benefits (monetary incentive to choose the hard option) and costs (effort required to receive the reward) when making a choice, while also assessing the dynamics of such choices in the form of response times (RT) distributions.

Nine individuals with PD treated with chronic STN DBS participated in the study (see Table S1 for patient characteristics and exclusion criteria). DA and STN DBS were manipulated within and across sessions in a pseudo-randomized order. During each session, participants made two alternative forced choices about whether to engage in low or high amounts of physical effort for monetary reward. Effort demands ("costs") were varied parametrically via the level of required manual grip force,[29,30] whereas "benefits" were varied via monetary reward (Figure 1). An initial "titration" phase offered individuals a range of choices, allowing us to assess individual participants' indifference points (where subjective benefits equal the subjective costs). A subsequent test phase was administered in which offers were systematically sampled on either side of the indifference point, facilitating more sensitive estimation of the impact of relative benefits (relBenefits) vs. relative costs (relCosts).[11] To ensure that any effects of treatment were not related to their core impact on motor function, maximum grip strength was recalibrated within each DBS /DA condition.[31]

Based on formal models, we predicted that DA and DBS would have dissociable effects on psychometric functions that are particularly prevalent around participants' indifference points (i.e., when the relative benefits of choosing the hard option equals the relative costs) (Figures 1B and 1C). We estimated participants' indifference points through the titration procedure, allowing us to determine the relative number of points (relBenefits) and relative effort levels (relCosts) for each offer relative to this indifference. Theoretical models[7,9,32] predict that striatal DA manipulations should asymmetrically alter the impact of benefits and

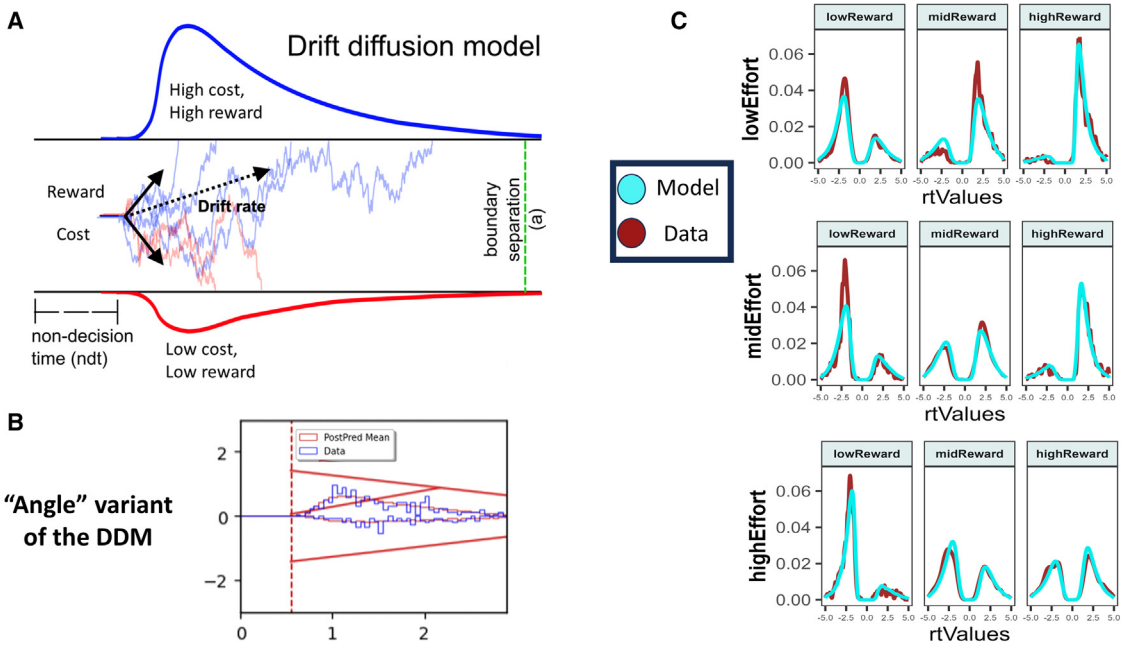

Figure 2. Computational model and posterior predictive check

(A) Illustration of drift diffusion model (DDM). The DDM was used to estimate how trial-by-trial changes in offered reward and cost (effort required) modulated the evidence accumulation (indexed by the drift rate [v]) toward the upper (hard effort high reward) or lower (low effort low reward) bound. The boundary separation parameter determines the amount of accumulated evidence required to commit to a choice (i.e., decision threshold). Basal ganglia models suggest DA will chiefly affect how rewards and costs map on to the drift rate whereas DBS will primarily result in a decrease in boundary threshold.

(B) Sample illustration of the angle variant of the DDM. The angle model contains an additional parameter (theta) which allows for a collapsing decision threshold as opposed to a static decision bound. Red lines show linearly decreasing bounds and an example fixed drift rate; blue histograms show expected response time (RT) distributions for choices to upper and lower boundary from one set of simulations. Adapted from Fengler et al.[35].

(C) The winning model's posterior predictive check (PPC) illustrates the model's (blue line) ability to capture empirical (maroon line) choice and RT distributions across different combinations of the hard choice's reward and effort levels. Simulations stem from model-derived parameters that best fit individuals' choices and RTs. For each panel, RT distributions to the right of 0 indicate choices of the hard option, and those to the left denote choosing the easy option.

See Figure S1 for detailed DA and DBS PPCs.

costs on choice, with DA increasing sensitivity to relative benefits but decreasing sensitivity to relative costs (Figure 1C). Conversely, if STN DBS lowers the decision threshold,[20,21,33] it should allow noise in value estimates to reduce choice consistency, shallowing the slope of psychometric choice function for both benefits and costs (and their differences, termed relValuation). We quantified these effects via logistic regression analyses assessing sensitivity to benefits and costs, before offering a more parsimonious computational process drift diffusion model that can simultaneously account for RT distributions that accompany these choices as a function of differing reward and effort levels.

To statistically evaluate these qualitative patterns (Figures 1B and 1C), we used linear mixed-effect models in which choice was modeled as a function of relBenefits and relCosts, DA, DBS, and their interactions (See STAR Methods section statistical modeling for details). Supporting theoretical predictions, a mixed-effects model (choice ~ benefits*DA + costs*DA) revealed that DA ON increased the contribution of benefits on choice while simultaneously decreasing the effect of costs (Figure 1D). Conversely, DBS lowered the impact of both benefits and costs (Figure 1B) in terms of the overall relValuation. Similar patterns were seen for both benefits and costs separately (Figure 1D). These patterns mirrored those expected from simulations, motivated by theoretical models of the basal ganglia, in which DA was assumed to asymmetrically alter the impact of benefits and costs on drift rate whereas DBS lowers decision threshold (Figures 1B and 1C; see supplemental information for model details). We further quantified these within-subject effects at the individual level by extracting each individual's estimated interaction coefficients from both mixed-effects models (see insets, Figures 1B and 1C). DA ON increased sensitivity to benefits ($T = 2.26$; $p < 0.024$) and decreased sensitivity to costs ($T = -1.81$; $p = .069$). Conversely, DBS reduced sensitivity to relValuation ($T = -4.17$; $p < .01$). These treatment effects amounted to a double dissociation: DA effects on benefits vs. costs were significantly greater than DBS effects ($T = 3.66$,$p < .001$), and vice versa for relValuation ($T = 4.75$,$p < .01$) (Figure 1D). Finally, although our core analyses focused on sensitivity to benefits and costs after adjusting for the patients' indifference point in their current DA/DBS state, we also confirmed that, as predicted, DA altered the indifference points themselves ($T = 3.16$; $p < .001$), increasing the sensitivity to benefits.

Although the above choice functions supported our initial predictions, models of decision dynamics are more diagnostic of the interpretations offered. For example, a reduced slope of a psychometric function as seen ON DBS could arise for a multitude of reasons, including attentional lapses or other sources of noise.[34] In contrast, if the effects are mediated by a change in

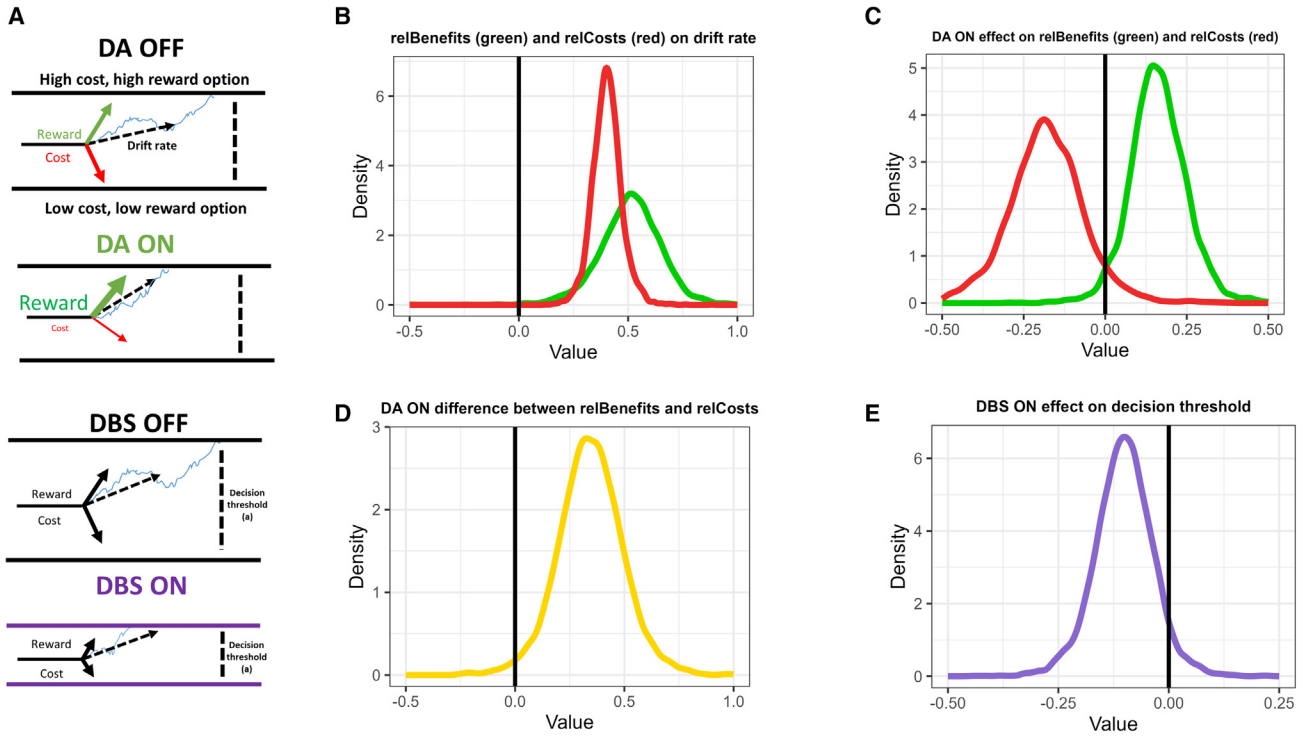

Figure 3. Predictions and selected posteriors from the winning computational model

(A) Theoretical DDM effects of DA ON (primarily increasing drift rate due to asymmetrical effect on benefits and costs) and DBS ON (lowering decision threshold).

Group posterior distributions for (B) relBenefits (green) and relCosts (coded as negative here, leading to a positive coefficient; red) on drift rate.

(C) Interaction terms showing DA ON increases sensitivity to relBenefits (green) and decreases sensitivity to costs (red) on drift rate.

(D) Within-subject difference between DA ON effect on relBenefits and relCosts, i.e., the difference between red and green from (C).

(E) DBS ON reduces decision threshold.

See Figure S1 for DA and DBS PPCs, Figure S2 for the group posterior effect of 4 hz stimulation on decision threshold, and Table S4 for individual participant drift diffusion model results.

decision threshold, these noisier choices should be accompanied by a distinct change to the decision dynamics, quantifiable with a sequential sampling model such as the drift diffusion model [DDM]). The DDM models decision making as an accumulation to a bound process, where the rate of accumulation ("drift rate") is determined by the strength of the evidence toward one boundary or another, and the boundary separation is the decision threshold. In the context of cost/benefit decision making, the drift rate is proportional to the relative benefits and costs of alternative options[11,28,35,36] such that relatively larger benefits should induce faster choices toward high effort and larger costs faster choices toward low effort. Around indifference, choices should not only be more equivocal but also slower and with heavier tails. Conversely, reductions in decision threshold should translate into noisier (less consistent) but also faster decisions, particularly around indifference. We tested the overall suitability of the DDM using hierarchical Bayesian estimation of the DDM (HDDM[16,35]). As predicted from *a priori* theory, the winning model allowed drift rate to vary by relBenefits, relCosts, and their interaction with DA status, and where decision threshold varied by DBS status.

Posterior predictive checks (PPC) confirmed that the DDM provided a good fit to the full spectrum of choices (Figure 2C). The density of choices showed peaked RT distributions for high-effort choices when benefits outweigh the costs, for low-effort choices when costs outweigh the benefits, and finally middling choices near indifference were associated with wider RT distributions for each option. Moreover, posterior distributions on model parameters confirmed the *a priori* hypotheses that DA status would alter the impact of benefits vs. costs on drift rate, whereas STN DBS would alter the decision threshold (Figure 3A). As expected, relBenefits and relCosts both affected drift rate (>99% group posterior probability for an effect different than 0. Costs (red) are coded as negative here, hence their impact on drift rate is positive) (Figure 3B). Critically, DA medication increased the impact of benefits on drift rate (Figure 3C green; interaction of DA on relBenefits 97% > 0) while simultaneously decreasing the impact of costs (Figure 3C red; interaction of DA on relCosts 95% < 0). These opposite effects complement the choice behavior analyses (Figure 1C) and offer additional evidence that modulating DA changes how individuals weigh costs and benefits during choice and their dynamics.[7,11,28] Conversely, STN DBS reduced the decision threshold (Figure 3D, 95% > 0), replicating several prior studies demonstrating that STN DBS reduces decision threshold in a variety of perceptual and value-based decision-making tasks,[20,21,33,37] as well as studies linking trial-by-trial variations in STN activity to decision threshold adjustments.[17,33,38] Moreover, allowing DBS status (manipulated within session) to alter the decision threshold improved model fit. Finally, we confirmed

that the impact of both DA and STN DBS on model parameters were consistent with posterior predictive checks on the patterns of choices and RT distributions (DA and DBS PPCs shown in Figure S1). Although DA induced a preference for high-effort choices as reward and effort increased, it also produced slower RTs when patients selected the low-effort option; these patterns were reproduced by the model (Figure S1A). Conversely, DBS induced more inconsistent choices and faster RT distributions near indifference, without impacting choices or RTs at the extremes (overall high or low value options), supporting the fixed-effects analysis reported above and ruling out alternatives that DBS induced more random choice across the board (Figure S1B).

DISCUSSION

These findings demonstrate dissociable impacts of DA and high-frequency STN DBS on distinct components of effort and value-based decision making within individual patients with PD. Whereas DA altered the relative sensitivity of benefits vs. costs of choice options, high-frequency DBS reduced the slope of the psychometric function. Moreover, these effects were manifested by distinct decision dynamics within the DDM. Evidence accumulation is faster toward rewarding options, an effect reflected in striatal electrophysiological data,[39] and DA accentuated this process while diminishing the sensitivity to costs. Conversely, DBS reduced the decision threshold, leading to faster but noisier choices around indifference point. Of note, these DBS effects did not meaningfully change when including DBS low-frequency blocks as well (see Figure S2; Table S2). DA and DBS's individual effects are consistent with previously reported data in the basic sciences on how DA alters benefits vs. costs of effort across species,[7,11,14] whereas high-frequency STN DBS dynamically interferes with the adjustment of decision threshold across tasks.[6,17,20,33,40] Our study builds on these results to show that these effects can be dissociated within individual participants by orthogonally varying DBS and DA status using a task designed to be maximally sensitive to these differences. Importantly, these effects cannot be attributed to raw effects of DBS and DA on motor function, as participants recalibrated their maximum grip strength for each DA and DBS condition (Figure S3).

Principally, these results suggest DA and DBS operate on separate nodes within the basal ganglia. Both DA and high-frequency DBS have been suspected of triggering impulsive behavior.[1,8,10] Our computational analysis suggests these effects are mediated by distinct decision processes and their dynamics even within the same individuals. In principle, such a computational biomarker may be useful for assessing underlying mechanisms of impulsive decisions in patients with PD and, potentially, other populations. However, while the within-subject design was powerful enough to reveal these distinct contributions, we recognize we do not have enough power to account for individual differences in the extent of these effects, which would require a much larger sample size. For example, participants exhibit differential effects of DBS on choice in both the qualitative and computational analyses, but it is impossible to assess whether these individual differences are related to theoretical reasons (such as electrode placements) or whether they simply reflect observation noise. Future work should focus on exactly how best to characterize individual reactivity to these treatments.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.cub.2023.12.045.

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AUTHOR CONTRIBUTIONS

G.J.P., W.F.A., and M.J.F. conceived the study and approved the methodology. G.J.P. ran the experiment, simulated and analyzed data, ran statistical and computational models, and wrote the paper with supervision from M.J.F and W.F.A. M.J.F. provided the funding.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Deposited data		
Empirical behavioral data	This paper	PDEffort_R_ready.csv: https://doi.org/10.5281/zenodo.10429624
Simulated behavioral data	This paper	dSim.csv: https://doi.org/10.5281/zenodo.10429624
Posterior predictive model data	This paper	ppcData_mAngleFinal.csv: https://doi.org/10.5281/zenodo.10429624
Posterior DDM model traces	This paper	TracesmAngleFinal.csv: https://doi.org/10.5281/zenodo.10429624
Software and algorithms		
MATLAB R2009a	MathWorks	www.mathworks.com
Psychtoolbox	Brainard and Vision[41]	http://psychtoolbox.org/
Behavioral analysis script	This paper	effortAnalysisFinal2023.R: https://doi.org/10.5281/zenodo.10429624
Computational DDM script	This paper	DDMScript.py: https://doi.org/10.5281/zenodo.10429624

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Guillaume Pagnier (guillaume_pagnier@brown.edu).

Materials availability

No new materials have been created.

Data and code availability

- Deidentified participant behavioral data have been deposited on zenodo.com. See key resources table for unique DOIs.
- Scripts for behavioral analyses and figure generation (using R) have been deposited on zenodo.com. We have also provided code to run the relevant computational models (using Python and HDDM). See key resources table for unique DOIs.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

METHOD DETAILS

Participants and experimental conditions

Eleven patients diagnosed with Parkinson's disease (PD) and implanted with a quadripolar electrode (model 3389, Medtronic Neurologic Division, Minneapolis, MN, USA) successfully completed both DA sessions (ON and OFF medication) on separate days (minimum 8 days apart; DA order randomized). All patients included here were implanted with the 3389 model non-directional lead. Two other patients (mean age 73.4 years) were excluded and did not complete the task due to clinical reasons (extreme fatigue and lack of task comprehension). The nine remaining patients (8 male, mean age 62.7years ± 3.6) were run at similar times during the day across sessions. All patients included here were programmed using non-directional contact settings. See Table S1 for detailed demographic information. All participants were referred to the study by neurologists who believed patients would be appropriate for behavioral testing. To screen for impulse control disorders, patients completed the Dickman Impulsivity Inventory-short (DII), a validated 23 item true/false questionnaire that measures impulsivity on two subscales: functional and dysfunctional impulsivity.[42] All patients exhibited low to normal values in both subscales. All participants were on dopaminergic medication and could tolerate performing the task OFF medication and OFF DBS. For the DA OFF sessions, patients were instructed to refrain from taking their DA medication for a minimum of 12 h beforehand.

For each participant, "DBS ON" was defined as the therapeutic high frequency stimulation setting. This study is also part of an ongoing exploratory project to characterize how different DBS settings (low/high frequency and ventral/dorsal electrode contact) influence effortful decision making. Our exploratory investigations have not led to consistent differences between ventral and dorsal or high vs. low frequency stimulation, potentially due to current spread and difficulty to isolate impacts of anatomical loci within STN. Thus, in this report we focus on the differential impacts of high frequency DBS ON/OFF vs. DA ON/OFF but for completeness we describe the full procedure here. For each DA session, patients played through each block of 105 trials five times in a pseudo-randomized order: **1)** DBS OFF **2)** therapeutic frequency dorsal stimulation **3)** 4hz dorsal stimulation, **4)** 4hz ventral stimulation, **5)**

therapeutic frequency ventral stimulation. Ventral stimulation involved stimulating at the most ventral contact possible. In these conditions, amplitude was lowered until the patient did not experience any side effects (this was not common). In the rare cases where the default therapeutic contact was more ventrally located, dorsal stimulation was done by stimulating the most dorsal contact. Our original goal in stimulating ventral vs. dorsal was to stimulate separate circuits within the STN (motor which is putatively stimulated by patients' more dorsal contacts and limbic which is thought to be a function of stimulating the more ventral contacts) however the lack of detailed imaging data for all patients as well as the fact that a few of our patients therapeutic contacts were ventrally located made disentangling the effect of location challenging, if not impossible. Importantly, for each session and DBS block, patients recalibrated their maximum force and re-titrated their indifference points, and thus all effects on indifference curves reported in the main text are relative to these newly defined indifference points, and not confounded by changes in overall motor function. DBS blocks were separated by a minimum of 5 min between blocks as a wash-out period. We did not find any evidence that DBS block order and session order affected any of the main results described above.

Task

Participants were run at Brown University (Providence, RI, USA) in a small room on campus designed for human data collection. Medical professionals were on standby in the unlikely instance of any adverse event. The task was written in MATLAB (Mathworks Inc, Natick, MA,USA; version R2009a) using the Psychtoolbox extension.[41] For each DBS block within each DA session, participants calibrated their maximum force, underwent the stepwise titration procedure, and performed the 105-test block phase. To calibrate, participants were asked to squeeze the dynamometer as hard as they could to turn a visual cue from black to green (the background for the entire experiment was a light gray). Participants' maximum force was calculated as the average of the three attempts.[43] Maximum force largely did not vary within patients (even across sessions and blocks), reducing the possibility that DA and DBS were significantly varying grip ability. On the first block, participants underwent an instructions block, during which they were introduced to the trial structure as well as the range of points they could be expected to receive (this was done to exclude any learning of what constitutes a "high" reward during the task. A trial was composed of a forced choice paradigm; participants had to choose between a low effort, low reward option (easy choice) and a high effort, high reward option (hard choice). The hard option offered either 460 or 520 points (a separate indifference point was calculated for each) while the easy option offered a range of points centered around participants' indifference points. A sample trial proceeded as follows: The easy option was denoted by the short bar while the hard option was denoted by the taller bar; a red line on the tall bar indicated the height participants needed to reach to receive the hard reward. During training, participants had to successfully demonstrate understanding of the tradeoffs between reward and effort by successfully completing several "catch trials": i.e., when the hard reward matched the easy reward (and thus choosing the easy option is the logical choice). This varied between two and ten practice trials. Afterwards, participants underwent a stepwise titration procedure to determine patients' block-specific indifference point, that is, how many points needed to be offered to render participants indifferent to the selected option for a given effort level. This titration procedure and how relative benefits/costs are calculated from these indifference points is adapted from the cognitive effort task.[11] A separate indifference point was calculated for easy trials (the red line denoting completeness was at 65% of participants MVC), medium trials (80% of MVC) and hard trials (95% of MVC). Patients then completed the test block (105 trials), in which the offered reward and effort amounts were sampled around each patients' indifference point. To avoid fatigue effects and maximize the number of decisions participants made in the allotted time, most trials did not actually require patients to "pay" the effort to receive whatever reward they chose. Instead, there was a 12% chance on any given trial (during the titration and test phases) that the participants did have to perform the effort they selected. Importantly, participants did not know prior to the decision whether they had to "pay" the effort to receive the reward. The amount they were paid at the end of study (in US dollars) was proportional to the total number of points they received across all the choices they made. DBS blocks and DA sessions were pseudorandomized across patients. Each DBS block within a DA session took about 20 min to complete.

QUANTIFICATION AND STATISTICAL ANALYSIS

Statistical modeling

Linear mixed-effects models were fit using the R package "lme4" were used to predict repeated-measures of choice (high effort/high reward option or low effort/low reward option) with fixed effects of either the difference between benefits and costs (relValuation; to test for the effects of DBS) or relBenefits and relCosts separately (to test our predictions for DA's opposing effects). In each of these models, we included the fixed effects as random effects as well and omitted intercepts from both the fixed and random effects. This was possible since the titration procedure converted absolute rewards and effort costs to relative benefits and relative costs for each individual for each DBS and DA condition. While our models predict DBS ON's' effect to be strongest on relValuation, we also predict DBS ON to lower sensitivity to both benefits and costs (as opposed to DA's opposing effects of increasing sensitivity to benefits and reducing costs). We ran an additional linear mixed-effects model to test this prediction as well as statistical models testing how low frequency (4 hz) stimulation affects relValuation (Table S2).

Computational modeling

We use the Python-based HDDM toolbox and the recent LAN extension to simulate and fit behavioral choices and response time distributions.[16,35] DDMs have been used extensively to study latent processes during value-based decision making, wherein

parameter estimates can be more informative about clinical status than the raw choices and RTs.[28] In these cases, the drift rate serves as a proxy for evidence accumulation towards the high reward, high effort option, with increasing drift when reward is high or effort is low. The decision threshold reflects the amount of evidence accumulated before committing to a decision, and typically varies with speed accuracy tradeoffs. Past work suggests DA modulates drift rate in a differential manner; DA ON boosts the impact of reward on drift rate while decreasing the impact of cost (effort level).[9,11,36] Separately, high frequency DBS has been shown to decrease decision threshold. Considering these findings, we simulated four conditions **1)** DA ON DBS ON **2)** DA ON DBS OFF **3)** DA OFF DBS ON **4)** DA OFF DBS OFF using a standard DDM (precise simulation parameters are located in Table S3). The number of simulated trials was comparable to the number of empirical trials.

Therefore, in line with our simulations our principal model (Figure 2) allowed drift rate to vary as a function of reward and effort amounts, with clear parametric effects of each observable in posterior parameter estimates and posterior predictive checks (Figure 3B). Model comparison was done by adding theoretically meaningful components and subsequently assessing whether (through posterior predictive checks and DIC) model fit was improved. We confirmed our *a priori* hypothesis that model fit improves if DA status impacted the influence of cost and benefits on drift rate, while DBS would impact decision threshold (Figure 3). Parameter convergence was inspected visually and Gelman Rubin statistics were less than 1.1 for all parameters in the final model represented in the main text (Figures 2 and 3). Final models were run with at least 20000 samples to ensure smooth posteriors.

We found that the data were better fit by a DDM with a linearly collapsing decision threshold (*Angle model*[35]) which is sensible in a task that includes choices near the indifference points (otherwise a decision maker might waste time accumulating trials with zero drift[44]), and thus all results are reported from this model (but all patterns observed in terms of impacts of DA and DBS were qualitatively similar in the fixed threshold model). Allowing the rate of collapse or starting point bias to vary by DBS and DA did not improve overall fit nor were the posteriors significantly different than 0.

The impact of DA and DBS can be seen not only in parameter estimates described in the main text but also in terms of their dissociable influences on choices and RT distributions for combinations of reward and effort levels. To visualize these effects, we simulated choices and RTs from the winning model using the posterior distributions of fitted model parameters (i.e., posterior predictive checks; Figure S1). This exercise confirmed that allowing DA to only influence drift rates and DBS to only influence threshold predicts dissociable patterns that were largely observed in the data. Specifically, while ON DA, patients showed greater preference for high effort options specifically when reward levels were high (highReward; DA PPC right column) and effort levels were high enough (midEffort and highEffort). The model captures these patterns and their RT distributions and makes a novel prediction when participants ON DA *do* make choices favoring the low effort option, they should actually be *slower* to do so (despite the common notion that DA speeds motor RTs). In the model, this results from a reduced impact of cost on drift rate and can be seen in both simulated and empirical data most evidently in the middle panel (midReward, midEffort) but also to a lesser extent (in both model and data) when the high effort choice was in the lowest effort ''lowEffort'' bin (top row, mid and high reward).

Conversely, the effect of DBS in the winning model is to reduce the decision threshold. Note that in the main text we reported that this effect, while consistent with several other reports in other domains,[6,19,20] was somewhat marginal (mean effect of DBS on threshold was 95% < 0). Inspection of the posteriors for individual subjects revealed that the reduction in decision threshold was clear in six out of nine individuals (See Table S4 for individual reports). Note that a lower decision threshold should impact choices when value differences are small (i.e., near indifference), and hence noise would have a larger impact on choice consistency. Indeed, one can see in model simulations from estimated parameters on DBS (where only decision threshold varied on vs. off DBS) induces more inconsistent choices and faster RTs specifically in the center row (mid effort) and confirmed empirically across that row. Importantly, the lowered threshold does not imply simply more random choice or lapses of attention; DBS does not induce more random choices when reward is high and effort is low or vice versa, and the model largely captures these patterns as well. Thus, both the winning computational model and the qualitative predictions highlight DBS differences to be centered around indifference. The finding that participants respond logically at subjective value difference extremes specificity helps preclude the possibility that DBS globally affects cognition - instead high frequency DBS ON lowers decision threshold but when evidence accumulation is so strong in one direction or the other, participants are still capable of making the optimal choice.