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Report

Reduction of Influence of Task Difficulty on Perceptual Decision Making by STN Deep Brain Stimulation

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Summary

Neurocomputational models of optimal decision making ascribe a crucial role—the computation of conflict between choice alternatives—to the subthalamic nucleus (STN) [1–3]. Specifically, these models predict that deep brain stimulation (DBS) of the STN will diminish the influence of decision conflict on decision making. In this work, patients with Parkinson's disease judged the direction of motion in random dot stimuli [4] while ON and OFF DBS. To induce decision conflict, we varied the task difficulty (motion coherence), leading to increased reaction time (RT) in trials with greater task difficulty in healthy subjects. Results indicate that DBS significantly influences performance for perceptual decisions under high decision conflict. RT increased substantially OFF DBS as the task became more difficult, and a diffusion model best accounted for behavioral data. In contrast, ON DBS, the influence of task difficulty on RT was significantly reduced and a race model best accounted for the observed data. Individual data fits of evidence accumulation models demonstrate different information processing under distinct DBS states. Furthermore, ON DBS, speed-accuracy tradeoffs affected the magnitude of decision criterion adjustment significantly less compared to OFF DBS. Together, these findings suggest a crucial role for the STN in adjusting decision making during high-conflict trials in perceptual decision making.

Results

Corticobasal ganglia (cortico-BG) networks control the expression of competing response alternatives and mediate decision making [5–8]. It has been reported that the subthalamic nucleus (STN) plays a central role in these networks during decision making [1, 2, 5, 6, 9, 10]. The STN is integrated in parallel motor and nonmotor cortico-BG thalamic loops, and distinct motor, limbic, and associative subterritories have been identified [11–13]. As a consequence, STN activity efficiently regulates the expression of actions as well as executive processes such as decision making [12, 14, 15]. Modulation of STN activity induced by deep brain stimulation (DBS) may thus influence cognitive, motor, and limbic circuits at the same time [15–17].

It has recently been suggested that the STN computes conflict between choice alternatives and mediates decision making accordingly [1, 2, 15]. Bogacz and colleagues [2, 3] outlined how cortico-BG networks can implement an optimal decision-making procedure, the multihypothesis sequential probability ratio test (MSPRT; cf. [18]). According to the MSPRT, sensory evidence is accumulated only as long as it is necessary to gain a required level of confidence. Thus, the MSPRT minimizes the decision time for any specified level of accuracy [18]. In the model of [2], information regarding the activity of sensory neurons selective for rightward motion affects the activity of neurons selective for leftward choices via the STN and vice versa (Figure 1A). For two alternatives, the MSPRT produces the same pattern of behavior as a diffusion model (Figure 1B) [18]. The decision mechanism integrates the difference between the accumulated evidence supporting the two alternatives until the evidence crosses a threshold (Figure 1B). Thus, according to the MSPRT model for cortico-BG networks, normal STN functioning results in decision behavior that is best described by a diffusion model [2]. On the contrary, under DBS, which disrupts information processing in the STN, resulting in impulsive decision making [15, 17], the MSPRT model predicts that DBS will make the activity of neurons selective for left choices more independent of sensory neurons selective for rightward motion. Furthermore, because STN neurons are the only highly nonlinear neurons in the MSPRT model, silencing of the STN results in activities of neural populations in the final stage of the model that are linearly proportional to the integrated evidence for the corresponding alternative (Figure 1C). Hence, under impaired STN computation, the resulting behavioral data should be best described by a simpler choice model, such as the race model, in which sensory inputs for the two alternatives are integrated independently [2, 3, 18]. We tested the prediction according to which DBS applied to STN decreases the effect of task difficulty during perceptual decision making [1–3, 15] by employing a direction-of-motion discrimination task (Figure 2). This prediction stems from the fact that reducing the difference in the two sensory inputs increases reaction times (RTs) to a larger extent when the inputs are integrated according to diffusion model (which integrates the difference between inputs) rather than the race model. Note that we induced decision conflict by means of task difficulty.

Behavior

With increasing stimulus coherence, participants were faster [$F(5,35) = 165.157$, $p < 0.001$] and more accurate [$F(5,35) = 451.842$, $p < 0.001$; Figures 3A and 3B], as with higher coherence the task was easier. The rate of change in RT as a function of coherence was lower when DBS was turned on (ON DBS) in the accuracy condition [Coherence * DBS: $F(5,35) = 24.182$, $p < 0.001$; Coherence * DBS * Instruction, $F(5,35) = 9.219$, $p < 0.001$; Figure 3B]. There was a similar but weaker effect on the slope

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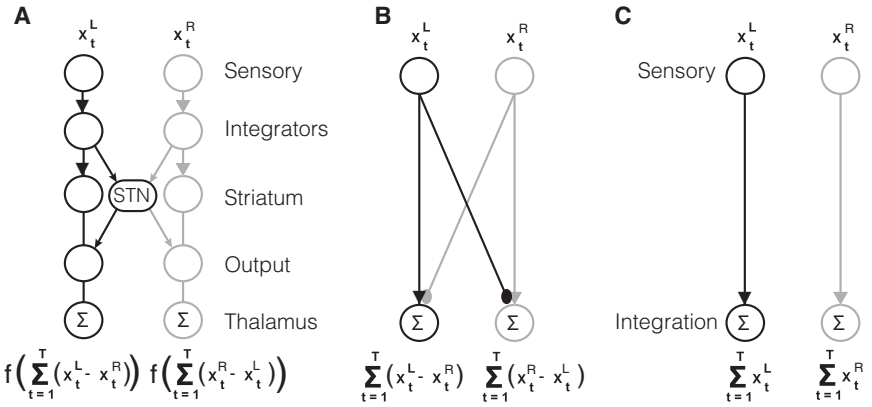

Figure 1. Computational Architectures for Models of Binary Decision Making

(A) A network implementing the MSPRT [3, 19]. The black and gray circles denote neural populations selective for movement toward the left and right, respectively. Labels next to the populations denote the brain areas where they are located ("Integrators" denotes cortical integrator neurons, and "Output" denotes the output nuclei of the BG: the internal segment of the globus pallidus and the substantia nigra pars reticulata). The arrows denote excitatory connections, and the lines ending with circles denote inhibitory connections. The labels above and below the models indicate the values of inputs and outputs, respectively. The labels x_T^L and x_T^R denote the activities of sensory neurons selective for motion toward the left and right, respectively, at the current time *T*. *f* is a monotonic function equal to $f(s) = -\log[1 + \exp(-gs)]$, where *g* is a positive model parameter and *s* the sum of the difference between both alternatives for each output unit.

(B) In the diffusion model, the difference between sensory inputs for the two alternative choices is integrated. A choice is made once this integrated difference exceeds a decision threshold. Only the difference between sensory inputs affects the values of the integrators.

(C) The simplest model of binary choice is the race model. Two independent integrators accumulate sensory evidence supporting each of the two choice alternatives (here, motion to the left or right). A choice is made once the activity of any integrator exceeds a fixed threshold.

See also Figures S2–S4 and S6–S8 and Tables S3–S5.

of accuracy as a function of coherence; it was less steep ON DBS during the accuracy condition [Coherence * DBS, $F(5,35) = 4.419$, $p = 0.003$; Coherence * DBS * Instruction, $F(5,35) = 9.219$, $p < 0.001$; Figure 3A]. In summary, DBS resulted in diminished effects of task difficulty on both the RT and accuracy in perceptual decision making, indicating that STN function is central to sensory-based action selection (Figure 3 and Figure S1 available online).

Under the speed instruction, participants had lower mean RTs [$F(1,7) = 135.039$, $p < 0.001$] and lower accuracy [$F(1,7) = 114.701$, $p < 0.001$; Figures 3A and 3B] compared to the accuracy instruction condition. The effect of instruction on RT was greater for low- than for high-coherence trials [Coherence * Instruction: $F(5,35) = 15.345$, $p = 0.001$). DBS appeared to affect the patients' overall response profiles, i.e., ON DBS patients were faster [$F(1,7) = 85.18$, $p < 0.001$] and less accurate [$F(1,7) = 120.627$, $p < 0.001$] compared to OFF DBS patients. The effect of instruction was greater during OFF DBS [DBS * Instruction: $F(1,7) = 6.329$, $p = 0.04$], which is consistent with models assuming a critical role of the STN in controlling the decision threshold [1, 15, 17].

On several coherence levels, some patients had the same accuracy OFF DBS with speed instruction and ON DBS with accuracy instruction. Figure S2 shows that when these patients' performance is compared on equal accuracy levels, they are actually faster OFF DBS than ON DBS (analogously to the way the diffusion model or MSPRT is faster than the race model when matched on accuracy; see Table S3).

To test whether our results could be related to motor deficits, we compared patients with Parkinson's disease to a group of age-matched controls (see Table S1).

Modeling

We fitted various MPSRT-derived versions of the race model and diffusion model to individual data sets and compared these models initially to a simple baseline model (assuming equal parameters across DBS conditions) and subsequently to more complex model instantiations (varying parameters between conditions; Figures S3 and S4; Tables S4–S8). As predicted, a diffusion model account better described the behavioral data in OFF DBS, whereas a race model account better described the behavior under DBS (Tables S4–S6 and S8). Additionally, to test the effects of DBS on decision thresholds, we estimated a so-called conflict model that implements separate thresholds for low-conflict and high-conflict trials (for details, see the Supplemental Experimental Procedures) and compared the magnitude of modulation between response instructions (Table S7). We found that DBS changed the degree to which subjects were able to adjust their decision thresholds

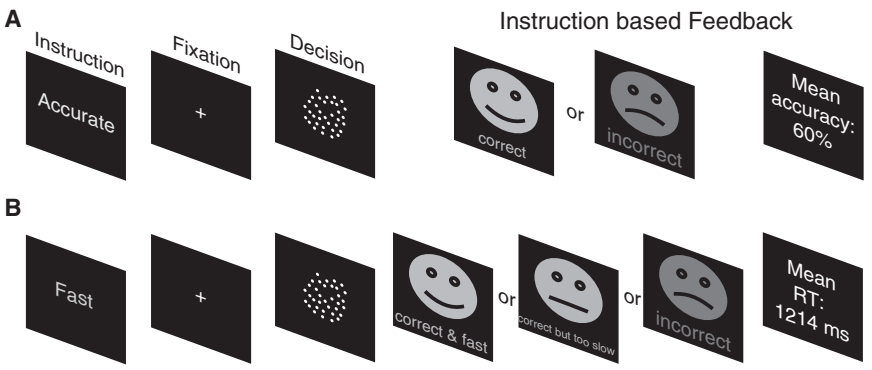

Figure 2. Experimental Design

(A) Accuracy instruction.

(B) Speed instruction.

Judgments were made in blocks of 20 trials randomly distributed over six levels of motion coherence, with speed or accuracy response instructions given at the beginning of each block. In each trial, participants had up to 2 s to respond. Either a response or the deadline terminated a trial. Participants received immediate feedback on each trial. See also Tables S2 and S5.

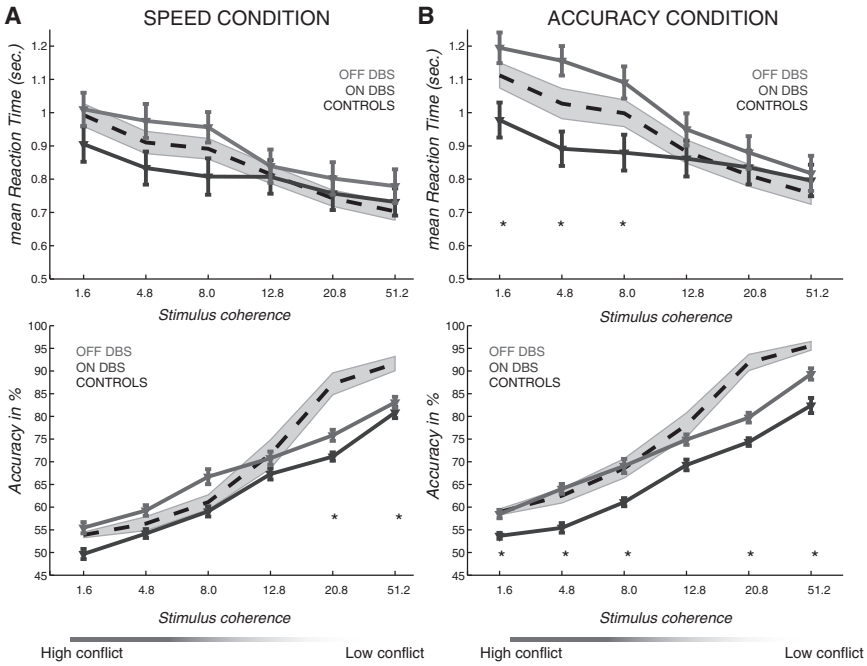

Figure 3. Behavioral Results

(A) Mean RT (top panel) and mean accuracy (bottom panel) as a function of stimulus coherence during the speed condition.

(B) Mean RT (top panel) and mean accuracy (bottom panel) as a function of stimulus coherence during the accuracy condition.

Dark-gray lines indicate ON DBS sample, broken black lines indicate control sample (shaded area represents the SEM), and light-gray lines depict OFF DBS sample. Error bars represent the SEM (dark gray, ON DBS; light gray, OFF DBS). Stars indicate significant differences between controls and PD patients on the specific coherence level. See also Figures S1–S4 and Tables S1–S3 and S5–S8.

for the low-coherence trials compared with the high-coherence trials [low < high: $t(7) = -3.9002$, $p = 0.0059$].

Discussion

Our results reveal a significant effect of STN DBS on perceptual decision making under task difficulty, supporting the assertion that cortico-BG networks implement system-level computations that optimize decision making [2, 3]. Individual data sets are well described by the race and diffusion models, accounting for changes in information processing under different DBS conditions, as predicted by the MSPRT model of cortico-BG network computations.

The top-down mechanism implementing adjustments of decision making under task difficulty appears to be too weak to overcome the automatic bottom-up computations of the BG network under DBS [15]. This is in line with previous findings in which the application of a race model to RT data from a DBS sample led to the interpretation that DBS (1) amplifies the descending cortical signals to the motor structures and (2) reduces the tonic background inhibition that suppresses unwanted premature responses [20].

The exact effects of DBS on the target structures are still unclear [21–23]. One idea is that under DBS, STN activity is influenced to a lesser extent by cortical input, which interferes with STN computations of the conflict in response to cortical signals representing alternative response plans. Furthermore, it seems paradoxical that DBS has effects similar to a suppression of STN activity in some tasks (e.g., [17] and this study) even though experimental data suggest that DBS activates axons of STN neurons [24]. A computational insight into this paradox is provided by the following idea: when DBS is turned on, the downstream neurons (e.g., in the thalamus) adapt their response threshold to increased STN activity so they can still transmit striatal inputs as if this constant STN input due to DBS were not present [25]. An alternative explanation is that DBS leads to suppression of the target area but an excitation of nearby fibers by way of a complex mechanism of inhibition (i.e., direct inhibition but also via inhibitory recurrent neurons that are excited by DBS) and excitation of efferent neurons to projection areas (i.e., STN projections and fibers of the internal globus pallidus) [23, 26].

The present data provide converging support not only for the MSPRT [2, 3] (Figure S2; Table S3) but also for other models proposing that the STN is involved in threshold regulation (which is not a prediction of MSPRT) [1, 15]. This illustrates the importance of considering and comparing different models of information processing for different states [19, 27] to account for the patterns of behavior.

In summary, we show for the first time that STN computations are crucial during perceptual decision making under task difficulty using a multi-method approach. We present empirical evidence in support of theories that suggest the cortico-BG networks' capacity for optimal computation of decision making under task difficulty.

Experimental Procedures

A detailed description of the experimental procedures, data analysis, and computational modeling can be found in the Supplemental Experimental Procedures. All participants gave informed consent to participate according to a protocol approved by the local ethics committee.

Supplemental Information

Supplemental Information includes Supplemental Experimental Procedures, four figures, and eight tables and can be found with this article online at http://dx.doi.org/10.1016/j.cub.2013.07.001.

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