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Report

Causal Role of Dorsolateral Prefrontal Cortex in Human Perceptual Decision Making

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Summary

The way that we interpret and interact with the world entails making decisions on the basis of available sensory evidence. Recent primate neurophysiology [1–6], human neuroimaging [7–13], and modeling experiments [14–19] have demonstrated that perceptual decisions are based on an integrative process in which sensory evidence accumulates over time until an internal decision bound is reached. Here we used repetitive transcranial magnetic stimulation (rTMS) to provide causal support for the role of the dorsolateral prefrontal cortex (DLPFC) in this integrative process. Specifically, we used a speeded perceptual categorization task designed to induce a time-dependent accumulation of sensory evidence through rapidly updating dynamic stimuli and found that disruption of the left DLPFC with low-frequency rTMS reduced accuracy and increased response times relative to a sham condition. Importantly, using the drift-diffusion model, we show that these behavioral effects correspond to a decrease in drift rate, a parameter describing the rate and thereby the efficiency of the sensory evidence integration in the decision process. These results provide causal evidence linking the DLPFC to the mechanism of evidence accumulation during perceptual decision making.

Results and Discussion

Perceptual decision making is the process of choosing one option or course of action from a set of alternatives based on information gathered from sensory systems. This process is often modeled as a temporal accumulation of sensory evidence to an internal decision threshold, which marks the commitment to a particular choice. Single-cell recordings in primates have identified this kind of accumulating activity in a distributed network of brain areas including the parietal and prefrontal cortices as well as the brain stem [2, 5, 6, 20, 21]. Similarly, results of human neuroimaging studies suggest that the integration of sensory evidence might involve regions of the parietal and prefrontal cortex [8, 9, 13, 22]. Despite the importance of these findings in advancing our understanding of the neural correlates of perceptual decision making, human studies have not yet provided causal evidence linking these candidate areas directly to the mechanism of evidence accumulation.

The major limiting factor in establishing this link has been the correlational nature of most neuroimaging methods, which provide no causal (i.e., interventional) evidence for the functional contribution of activated brain regions to a particular task or underlying neuronal process. Similar to electrical microstimulation in primates [23, 24], transcranial magnetic stimulation (TMS) in humans has the potential to circumvent this limitation. Here, we capitalize on this technique and introduce a novel approach that combines repetitive TMS (rTMS) and computational modeling to help establish the missing causal link between prefrontal cortex and the process of evidence accumulation during human perceptual decision making.

On the one hand, low-frequency rTMS can transiently disrupt the function of an area by depressing cortical excitability, potentially leading to quantifiable behavioral consequences [25–27]. Mathematical models, on the other hand, can characterize the computational principles underlying the cognitive process under investigation by defining internal variables that instantiate these computations. By combining the two approaches, one could ultimately describe the behavioral effects resulting from rTMS in terms of the model's internal variables, thereby providing a direct link between the stimulated area and the function ascribed to these variables.

We adopted this approach to study the involvement of the dorsolateral prefrontal cortex (DLPFC) during perceptual decision making using a task explicitly designed to induce a temporal integration of sensory information (see below). We chose the target site based on previous reports by Heekeren and colleagues [8, 9], who suggested that a region in the left posterior DLPFC might integrate the incoming sensory evidence, independent of stimulus and response modalities. We hypothesize that for this region to be causally linked to the process of evidence accumulation, rTMS applied to this area should hinder behavioral performance relative to a sham condition. Moreover, when modeled with the drift-diffusion model (DDM) for simple decision making (a well-established model in cognitive psychology [12, 17, 28]), these behavioral effects should be explained primarily by changes in drift rate, a model's internal variable that quantifies the rate, and hence the efficiency, of sensory evidence integration.

For each of 12 well-trained participants, we applied two separate 12 min rTMS sessions: a 1 Hz low-frequency rTMS to the left DLPFC (Montreal Neurological Institute coordinates: −22, 26, 36; Figure 1A) and a 12 min sham rTMS over the same area. After each rTMS session, participants completed four trial blocks, each lasting around 5 min, of a speeded perceptual categorization task (Figure 1B). Specifically, we used a face-versus-car categorization task designed to induce a time-dependent accumulation of sensory evidence based on concrete perceptual categories through rapidly updating dynamic stimuli. We used two levels of sensory evidence (high and low). Participants indicated their choice via a button press

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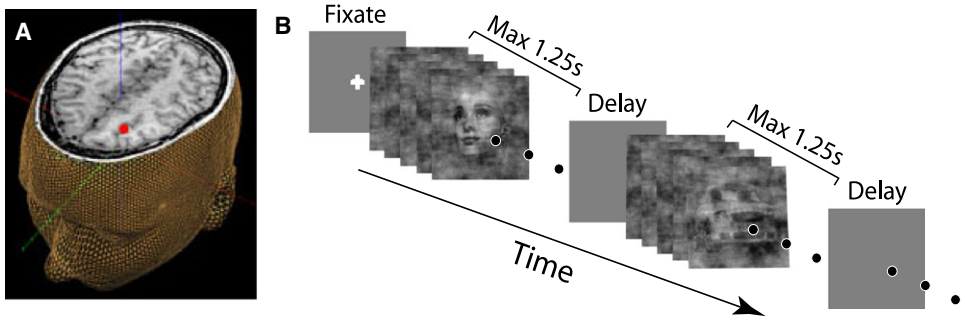

Figure 1. rTMS Target Site and Behavioral Task

(A) A region within the superior frontal sulcus, in the left dorsolateral prefrontal cortex (MNI coordinates: −22, 26, 36; red circle), as reported previously by Heekeren and colleagues [8, 9] using functional magnetic resonance imaging experiments.

(B) Schematic representation of the behavioral task. See Supplemental Experimental Procedures for more details.

as soon as they had formed a decision. To account for potential confounding effects of learning, we counterbalanced the order of rTMS and sham sessions across participants (see Supplemental Results available online for more details). Importantly, the presence of multiple trial blocks per session served as an additional control because we anticipated potential rTMS effects to dissipate over time (i.e., during the second half of trials) [29, 30]. Therefore, for all analyses we split the trials into a first half (i.e., the first two trial blocks) versus a second half (third and fourth blocks).

First, we looked at the overall behavioral effects (accuracy and mean reaction times). As expected, we found a significant main effect of sensory evidence on both the accuracy and mean reaction time. Specifically, there was an increase in accuracy and a decrease in mean reaction time in the high- relative to the low-stimulus sensory evidence condition for both the first ($F_{1,10} = 103.26$, $p < 1 \times 10^{-4}$ and $F_{1,10} = 99.823$, $p < 1 \times 10^{-4}$, respectively; Figures 2A and 2C) and second half of trials ($F_{1,10} = 36.662$, $p < 1 \times 10^{-4}$ and $F_{1,10} = 218.889$, $p < 1 \times 10^{-4}$, respectively; Figures 2B and 2D). Additionally, note that there was a trend for an overall increase in mean response time as a function of time (i.e., Figures 2C and 2D), possibly as a result of participant fatigue in the course of each session (see Supplemental Results).

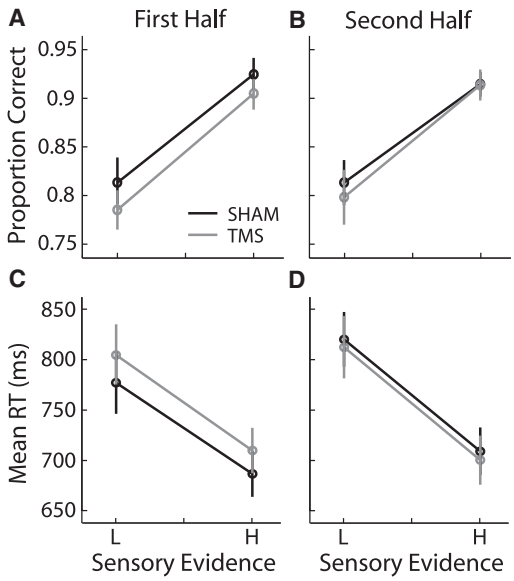

Figure 2. Behavioral Performance

Mean accuracy (A and B) and mean response time (RT) (C and D) across participants for the two levels of sensory evidence (L, low; H, high) and for each of the rTMS and sham conditions, separately for the first (A and C) and second half (B and D) of trials. Error bars represent standard error of the mean.

Crucially, in keeping with the main focus of our study, we also found a main effect of TMS on behavior for the first but not the second half of trials. Specifically, immediately after rTMS was administered to the left DLPFC (i.e., during the first half of trials), accuracy was significantly reduced ($F_{1,10} = 6.326$, $p = 0.0306$) and mean response times were significantly increased ($F_{1,10} = 6.474$, $p = 0.0291$) relative to the sham condition (Figures 2A and 2C). There was no significant interaction between TMS and the level of sensory evidence in either accuracy or response time ($F_{1,10} = 0.382$, $p = 0.5503$ and $F_{1,10} = 0.329$, $p = 0.5792$, respectively), suggesting that rTMS affected performance similarly across our two stimulus difficulty levels (but see Supplemental Results). These behavioral effects were no longer present in the second half of trials ($F_{1,10} = 0.849$, $p = 0.3785$ and $F_{1,10} = 0.816$, $p = 0.3876$, respectively; Figures 2B and 2D), confirming our original hypothesis that the rTMS effects would dissipate over time [29, 30].

Next, we fit the DDM [12, 17, 28] to the behavioral data from individual participants, separately for the first and second half of trials in each of the rTMS and sham sessions (see Supplemental Experimental Procedures). In short, the DDM assumes a stochastic accumulation of sensory evidence over time, from a starting point to one of two decision boundaries corresponding to the two choices. The model decomposes accuracy and response times into components of processing that reflect the rate of evidence accumulation (drift rate), the amount of evidence required to make a decision (starting point and decision boundaries), and the duration of nondecision processes (nondecision time), such as early stimulus encoding and response production along with the variance in each of the components of processing.

Our DDM results revealed that drift rate and nondecision time were the two parameters that systematically varied across experimental conditions for all of our subjects (see Supplemental Experimental Procedures and Tables S1 and S2). In line with what we have reported previously [12, 18], there was a main effect of the level of sensory evidence on drift rate, such that drift rate was higher for high relative to the low sensory evidence condition, for both the first and second half

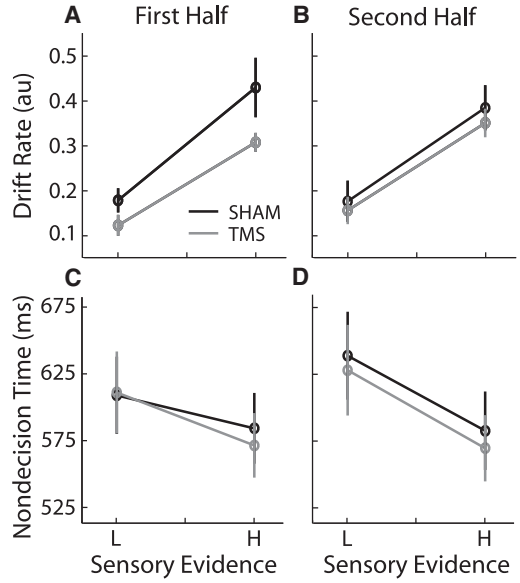

Figure 3. Diffusion Model Parameter Estimates

Mean drift rate (A and B) and mean nondecision time across participants for the two levels of sensory evidence (L, low; H, high) (C and D) and for each of the rTMS and sham conditions, separately for the first (A and C) and second half (B and D) of trials. Error bars represent standard error of the mean. See also Figures S1 and S2 to visualize the overall quality of the drift-diffusion model fits.

of trials ($F_{1,10}$ = 54.482, $p < 1 \times 10^{-4}$ and $F_{1,10}$ = 20.324, p = 0.0011, respectively; Figures 3A and 3B), confirming that evidence accumulation is faster and more efficient for easier than harder trials. There was also a main effect of sensory evidence on nondecision time such that nondecision time was shorter for high relative to the low sensory evidence condition, for both the first and second half of trials ($F_{1,10}$ = 16.168, p = 0.0024 and $F_{1,10}$ = 24.350, p = 0.0006, respectively; Figures 3C and 3D), suggesting that early stimulus encoding was faster for easier (i.e., high-evidence) trials.

Central to our study, we also found a main effect of TMS on drift rate for the first but not the second half of trials. Specifically, immediately after rTMS was administered to the left DLPFC (i.e., the first half of trials), the drift rate was significantly reduced relative to the sham condition ($F_{1,10}$ = 6.296, p = 0.031; Figure 3A). There was no significant interaction between TMS and level of sensory evidence ($F_{1,10}$ = 0.929, p = 0.3578). As expected, the TMS effects were eliminated in the second half of trials ($F_{1,10}$ = 0.637, p = 0.4434; Figure 3B). Importantly, no corresponding differences were found for nondecision time for either the first or the second half of trials ($F_{1,10}$ = 0.344, p = 0.5702 and $F_{1,10}$ = 3.226, p = 0.1, respectively; Figures 3C and 3D), indicating that behavioral effects resulting from rTMS are exclusively captured by changes in drift rate. These findings were additionally confirmed by a fully flexible fitting procedure on the DDM parameters (Supplemental Experimental Procedures).

One important consideration is whether our results might reflect a disturbance of top-down attentional control on sensory systems or of semantic processing, as opposed to a direct influence on decision making, because DLPFC has also been implicated in these processes [31–34]. Importantly, reduced top-down influence of attention on sensory cortex as a result of rTMS would have prolonged the early encoding of the stimulus, which in turn would have resulted in increased nondecision times [35] in the TMS relative to the sham condition. Crucially, there were no significant differences in nondecision times between TMS and sham in our task (Figure 3C). Additionally, there are clear anatomical and functional dissociations between the region of the left DLPFC that we targeted here and those involved in attentional control [31, 34, 36–38] and semantic processing [32, 33, 39, 40] (see Supplemental Results and Supplemental Discussion for more details). Taken together, these results render a purely attentional or semantic account of our effects unlikely.

The ultimate goal of research on human decision making is to provide a comprehensive account of the networks involved in this process. An interesting question for future work is whether altering activity of other regions (e.g., in parietal cortex) might also influence the decision process and, if so, whether these other areas interact with DLPFC to give rise to some of the observed effects. Similarly, one would need to address whether DLPFC is directly involved in computing the integration of the incoming evidence or whether it merely reflects the output of this computation. Despite these caveats, however, our rTMS-induced effects provide strong evidence for a causal role of the left DLPFC in affecting how efficiently the accumulated evidence is represented and ultimately used to make a decision. Combining TMS with neuroimaging might provide a good conduit to addressing these open questions [41–43].

In conclusion, our results show that decision-making mechanisms, inter alia, can be traced and studied in left DLPFC. More specifically, they demonstrate that for nominally identical stimuli, transient inhibition of the left DLPFC hampers, explicitly, the rate and ultimately the efficiency with which sensory evidence is integrated. As such, these findings provide the first causal evidence linking left DLPFC to the mechanism of evidence accumulation during perceptual decision making in humans. Importantly, these results were afforded by our model-based TMS approach, which, as we demonstrated here, has the potential to become a powerful tool in cognitive neuroscience.

Supplemental Information

Supplemental Information includes Supplemental Results, Supplemental Discussion, Supplemental Experimental Procedures, two tables, and two figures and can be found with this article online at doi:10.1016/j.cub.2011.04.034.

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