Causal evidence for frontal cortex organization for perceptual decision making

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Although recent research has shown that the frontal cortex has a critical role in perceptual decision making, an overarching theory of frontal functional organization for perception has yet to emerge. Perceptual decision making is temporally organized such that it requires the processes of selection, criterion setting, and evaluation. We hypothesized that exploring this temporal structure would reveal a large-scale frontal organization for perception. A causal intervention with transcranial magnetic stimulation revealed clear specialization along the rostrocaudal axis such that the control of successive stages of perceptual decision making was selectively affected by perturbation of successively rostral areas. Simulations with a dynamic model of decision making suggested distinct computational contributions of each region. Finally, the emergent frontal gradient was further corroborated by functional MRI. These causal results provide an organizational principle for the role of frontal cortex in the control of perceptual decision making and suggest specific mechanistic contributions for its different subregions.

perception | frontal cortex | hierarchy | TMS | fMRI

The frontal cortex has extensive connections with most other cortical and subcortical structures, placing it in a unique position to orchestrate a wide range of processes (1). Even though, historically, only a few studies have investigated the involvement of the frontal cortex in perceptual processes, a large amount of recent research has demonstrated that the frontal cortex has a critical role in the control of perceptual decision making (2–5). Despite these empirical findings, the unique contributions of different functional subdivisions within frontal cortex for perceptual decision making remain underspecified.

We propose that a frontal organization for perception emerges when one considers the temporal structure of perceptual decision making. Perceptual judgments consist of subsequent stages, such as selection, criterion setting, and evaluation processes (3, 4, 6). Here, we use the term "selection processes" to refer to mechanisms that allow the individual to direct resources to a specific object, feature, or part of space; "criterion setting processes" to refer to mechanisms that allow the individual to exert control over the final perceptual decision by adjusting the criteria for making the decision; and "evaluation processes" to refer to mechanisms that allow the individual to determine the likelihood that a perceptual judgment was correct. The temporal dependency between these three processes is evident when considering that the stimulus needs first be selected before decision criteria can be applied, and that both of these processes need to occur before evaluation can fully take place. It is likely that these processes partially overlap in some cases (e.g., criterion setting can be initialized, even if not fully completed, before the stimulus selection has concluded), but such partial overlaps do not undermine the general temporal structure of these three processes.

How is the frontal cortex organized to support and control these three stages of perceptual decision making? Several organizational principles of the frontal cortex have emerged in recent years. Notably, convergent evidence points to a rostrocaudal (i.e., anterior-to-posterior) gradient in the frontal cortex such that rostral regions support more abstract representations that build on the representations in caudal areas (1, 7–10). In particular, Fuster and Bressler (11) argue that progressively rostral regions are critical for progressively later stages of the perception/action cycle. Despite the emphasis on both perception and action, this representational structure of the frontal cortex has been studied virtually exclusively with regard to cognitive control over action, and has not directly been linked to the processes underlying perceptual decision making. We address this gap and specifically investigate whether selection, criterion setting, and evaluation processes necessary for perceptual decision making are controlled by the caudal, midlateral, and rostral frontal cortex, respectively.

Most research on the role of frontal cortex in perception has thus far been correlational. However, because the same regions of frontal cortex often support a variety of cognitive functions (1), such studies cannot conclusively establish the degree of specialization of different subregions of frontal cortex. In addition, previous studies have typically focused on a single one of these three perceptual processes, and thus could not directly compare their dependence on regions within the frontal cortex.

Here, we move beyond these limitations, and use causal techniques to explore the theoretically driven question of whether successive perceptual processes are controlled by progressively rostral regions of the frontal cortex. We designed a strong test of this hypothesis by a priori defining for each subject three regions along the lateral frontal cortex that are involved in the three proposed perceptual decision-making processes, and then targeted these regions with transcranial magnetic stimulation (TMS) to disrupt their function. This causal approach allowed us to move beyond previous correlational studies, which have found widespread frontal cortex activity during perceptual decision-making

Significance

The frontal cortex has long been understood as the seat of higher level cognition. Recent research, however, highlights its role in modulating perception. Here, we present a theoretical framework for frontal involvement in perceptual decision making and test it with the causal technique of transcranial magnetic stimulation. We find that progressively rostral regions of frontal cortex are involved in the control of progressively later stages of perceptual decision making. These causal findings are further corroborated by functional MRI and simulations of a dynamic model of decision making. Our results point to a critical role of the frontal cortex in the control of perceptual processes and reveal its intrinsic organization in support of modulating perception.

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tasks (12), and to test directly the necessity of each region for the control of each processing stage. Our task required subjects to deploy spatial attention to engage selection processes (6), follow speed/accuracy instructions to engage criterion setting processes (13), and provide metacognitive judgments to engage evaluation processes (14). We found clear evidence for frontal cortex organization such that progressively rostral regions were necessary for controlling later stages of processing during perceptual decision making. This emergent gradient was corroborated by simulations derived from a dynamic model of decision making that suggested specific computational contributions of each frontal region, as well as functional MRI (fMRI) data that extended the TMS results.

Results

We designed a task in which the processes of selection, criterion setting, and evaluation could be clearly identified (Fig. 1*A*). On each trial, subjects were instructed to attend selectively to one of two peripheral stimuli (selection). The task was to indicate the orientation (clockwise/counterclockwise) of a grating embedded in noise while adjusting the decision criterion so as to emphasize either speed or accuracy (criterion setting). After making their choice, subjects indicated their level of confidence (evaluation).

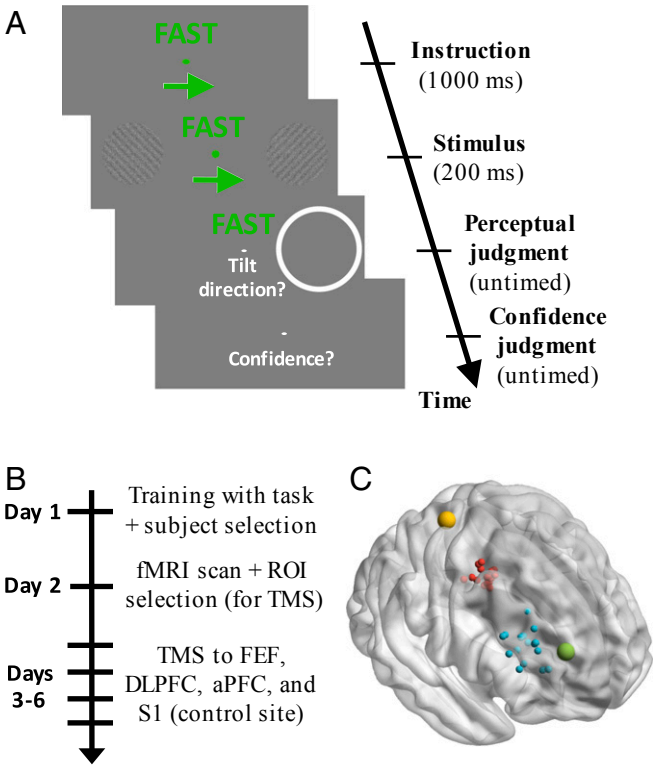

Fig. 1. Task, experiment time line, and TMS locations. (*A*) Trial sequence. Each trial began with a 1-s instruction to attend to either the left or right stimulus, as well as to emphasize either speed or accuracy. The grating stimuli were presented for 200 ms, and a postcue indicated which stimulus subjects should respond to. The postcue was on the attended side 66.7% of the time. Responses regarding stimulus orientation (clockwise/counterclockwise) and confidence (on a 1–4 scale) were untimed. The following trial began 1 s later. (*B*) Experiment time line. ROI, region of interest. (*C*) Approximate location of S1 is depicted in yellow (the target was identified in the postcentral gyrus). FEF (red) and DLPFC (blue) were localized separately for each subject based on individual fMRI activations (each dot represents a different subject). Finally, the site for aPFC stimulation (green) was common across subjects and based on Fleming et al. (4). All targets were identified in the right hemisphere. The *y* coordinates for each region did not overlap: S1: −33, FEF: [−10, 2], DLPFC: [26, 48], aPFC: 53.

Each subject received training (day 1), then performed the task during the collection of fMRI data (day 2), and finally received TMS to one of four different sites before performing the same task (days 3–6; Fig. 1*B*). Based on the fMRI data, for each subject, we identified three progressively more rostral sites in frontal cortex: putative frontal eye fields (FEFs), dorsolateral prefrontal cortex (DLPFC), and anterior prefrontal cortex (aPFC), as well as the primary somatosensory cortex (S1), which served as a control site (Fig. 1*C*). We then delivered continuous theta-burst stimulation (cTBS) to each of these regions for each subject on different days. cTBS has been demonstrated to produce a decrease in the excitation level in the stimulated cortex (15), likely through processes akin to long-term depression.

TMS Evidence for Frontal Organization for Perception. TMS did not influence overall task performance as measured by overall accuracy, reaction time (RT), or confidence ($P > 0.05$ for all pairwise comparisons between any of the four sites; Table S1), suggesting it is unlikely that frontal cortex is necessary for the low-level visual processing. We now turn to the frontal cortex involvement in the control of selection, criterion setting, and evaluation processes.

Selection (spatial cue). The first critical component of the task was a requirement to control the way stimuli were selected for processing: a cue indicated which of two stimuli to attend. Subjects successfully followed the spatial cue as demonstrated by faster RTs for attended compared with unattended stimuli during the fMRI session [RT difference = 128 ms, $t(16) = 8.52$, $P = 2 * 10^{-7}$]. A decreased ability to engage this selection process following TMS would manifest itself as a smaller RT difference between attended and unattended stimuli (6). We predicted that TMS to the most caudal frontal site (putative FEF) would exhibit this effect based on previous work (reviewed in 16). Consistent with this prediction, we found a significant difference in performance between different TMS sites [$\chi^2(3) = 10.6$, $P = 0.01$, mixed-effects model (17); Fig. 2*A*]. A planned post hoc *t* test confirmed that the RT difference between attended and unattended stimuli was significantly decreased after FEF stimulation compared with the control site [RT difference = 102 ms, $t(16) = 2.89$, $P = 0.011$], corresponding to an effect size of d = 0.7. Exploratory analyses also demonstrated a significant difference in this selection effect between FEF TMS and both DLPFC TMS [RT difference = 77 ms, $t(16) = 2.25$, $P = 0.039$, d = 0.55] and aPFC TMS [RT difference = 75 ms, $t(16) = 3.1$, $P = 0.007$, d = 0.75]. No significant differences were found between S1, DLPFC, and aPFC ($P > 0.05$ for all pairwise comparisons, RT differences < 28 ms). Thus, these findings strongly suggest that the selection process depends on the caudal frontal cortex (putative FEF) but not on the more rostral frontal regions.

Criterion setting (speed/accuracy instruction). The second critical component of the task involved a requirement to set a perceptual criterion by emphasizing on different trials either speed or accuracy. Such adjustment of the response threshold has long been considered an important example of how decision criteria are set in perceptual decision making (5, 13). Subjects successfully followed the instructions as demonstrated by a large RT difference between accuracy and speed trials during the fMRI session [RT difference = 370 ms, $t(16) = 5.19$, $P = 9 * 10^{-5}$]. A decreased ability to set the response criterion appropriately would manifest in a smaller RT difference between the two types of trials. We predicted that TMS to the middle of the rostrocaudal frontal gradient (DLPFC) would interfere with the control of the criterion setting process, based on previous work (5). Consistent with this prediction, we found a significant difference in performance between different TMS sites [$\chi^2(3) = 15.3$, $P = 0.002$, mixed-effects model; Fig. 2*B*)]. A planned post hoc *t* test confirmed that the RT difference between accuracy and speed instructions was significantly decreased following DLFPC TMS compared with the control site [RT difference = 55 ms, $t(16) = 3.31$,

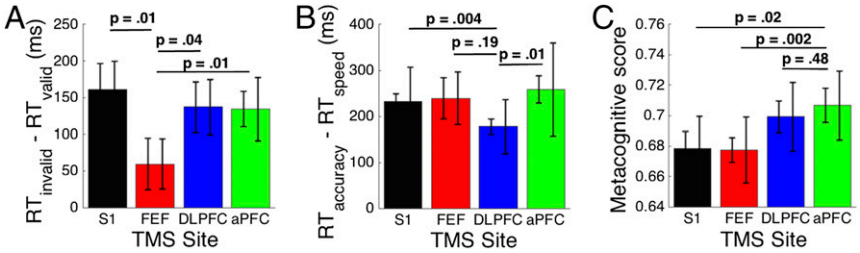

Fig. 2. TMS results. (*A*) TMS to FEF decreased subjects' ability to follow the spatial cue, as quantified by the RT difference between unattended and attended stimuli. (*B*) TMS to DLPFC decreased subjects' ability to follow speed/accuracy instruction, as quantified by the RT difference between accuracy and speed trials. (*C*) TMS to aPFC increased subjects' metacognitive scores, as quantified by the Type 2 AUC curve. The increase was similar but smaller for DLPFC. The left error bars represent the within-subject SE for the comparison with FEF (*A*), DLPFC (*B*), and aPFC (*C*). The error bar for the comparison site is the same as the S1 error bar. The right error bars represent the between-subject SE, and are not indicative of the significance of the effects.

$P = 0.004$, d = 0.8]. Exploratory analyses also demonstrated a significant difference in this effect between DLPFC TMS and aPFC TMS [RT difference = 81 ms, $t(16) = 2.74$, $P = 0.01$, d = 0.66] but not between DLPFC TMS and FEF TMS [RT difference = 62 ms, $t(16) = 1.38$, $P = 0.19$, d = 0.34]. No significant differences were found between S1, FEF, and aPFC ($P > 0.05$ for all pairwise comparisons, RT differences < 27 ms). These results suggest a critical role for DLPFC (located in the middle part of the rostrocaudal gradient in frontal cortex) in the control of the criterion setting process.

Evaluation (metacognitive ratings). The third critical component of the task required subjects to evaluate their perceptual judgments by providing a confidence rating. We investigated the extent to which these confidence ratings were linked to subjects' accuracy, which is a measure of subjects' metacognitive ability. This correspondence was determined as the area under the type 2 receiver operating characteristic curve (Type 2 AUC) (18) (*Materials and Methods*). We predicted that TMS to the most rostral area of frontal cortex (aPFC) would impair subjects' metacognitive scores, based on previous work (4, 18). However, the observed effect was in the opposite direction such that TMS to the rostral part of frontal cortex improved metacognition. Indeed, we found a significant difference in Type 2 AUC between different TMS sites [$\chi^2(3) = 11$, $P = 0.01$, mixed-effects model; Fig. 2*C*]. A planned t test demonstrated that the metacognition score was significantly higher after aPFC TMS compared with the control site [Type 2 AUC difference = 0.03; $t(16) = 2.51$, $P = 0.02$, d = 0.61]. Exploratory analyses showed that subjects' metacognitive scores were also higher after aPFC TMS compared with FEF TMS [Type 2 AUC difference = 0.03; $t(16) = 3.61$, $P = 0.002$, d = 0.88], although there was no significant difference between TMS to aPFC and DLPFC [$t(16) = 0.72$, $P = 0.48$, d = 0.17]. Comparing the other three sites (S1, FEF, and DLPFC), we found that TMS to DLPFC led to significantly higher metacognitive scores compared with TMS to FEF [Type 2 AUC difference = 0.02; $t(16) = 2.39$, $P = 0.03$, d = 0.58], although no significant differences were found in the other two comparisons ($P > 0.05$ in both cases).

The finding that TMS to DLPFC affected metacognition, despite our prediction that only TMS to aPFC would do so, could be partly due to the fact that DLPFC was localized in a very anterior location for most subjects (Fig. 1*C*). Thus, this finding does not necessarily contradict the possibility that metacognitive sensitivity depends primarily on the rostral part of frontal cortex.

Due to our unexpected findings (aPFC TMS leading to improved rather than impaired metacognitive performance), we sought to confirm that our results were not due to the specific measure of metacognition that we chose. We repeated our analyses with three more measures: meta-d′ (19), a simple correlation between confidence and accuracy [also known as phi (20)], and the difference in confidence between correct and incorrect trials. All three measures showed the exact same pattern of results (Table S2). Specifically, aPFC TMS led to significantly higher metacognitive scores than both the control site and FEF for each measure ($P <$ 0.05 in all cases).

Comparing the three measures. The three results above suggest a selective association between FEF, DLPFC, and aPFC and the processes of selection, criterion setting, and evaluation in perceptual decision making, respectively. To corroborate this conclusion further, we found a significant interaction [$\chi^2(6) = 16.3$, $P = 0.01$, mixed-effects model] between the TMS site (S1, FEF, DLPFC, and aPFC) and the task component (selection, criterion setting, and evaluation). However, because not all pairwise comparisons were significant for each measure, we cannot conclude the existence of a complete triple dissociation among these three regions.

Simulating the TMS Effects with a Dynamic Model of Decision Making. Our results suggest that caudal, middle, and rostral frontal cortex have differential contributions to perceptual decision making. To understand the functional role of each region better, we performed simulations using an adapted model of perceptual decision making introduced by Kepecs et al. (21) and De Martino et al. (22), wherein evidence is accumulated separately for each of the two choices, and the decision is made when one of the accumulators reaches a bound (23). Confidence is then assigned as the noise-corrupted difference between the winning and losing accumulators (Δe, the difference in evidence; Fig. 3*A*) such that higher difference indicates higher confidence. The critical parameters of the model are (*i*) the drift rate, which determines how quickly evidence accumulates for each choice; (*ii*) the bound, which determines how much evidence is needed to make a decision; and (*iii*) the confidence noise, which determines the strength of the association between confidence and accuracy.

This modeling framework provides a natural way to operationalize the processes of selection, criterion setting, and evaluation using the above parameters (Fig. 3*A*). First, selection is defined as the process of enhancing the sensitivity for one stimulus over another. In the framework of our model, this process is equivalent to boosting the drift rate for the correct choice for the attended, but not the unattended, stimulus. Second, the requirement to set the response criterion according to the speed/accuracy instructions is naturally modeled by an adjustment of the bound to be higher for accuracy compared with speed instructions. Third, we observed significant variability in the metacognitive scores (from 0.58 to 0.83 in the fMRI session), which points to the existence of confidence noise that varies between subjects (22). This confidence noise controls how tightly the metacognitive ratings follow a subject's decision accuracy such that a greater amount of this type of noise leads to lower metacognitive scores.

Our simulations demonstrated that changes to these three parameters of the model can qualitatively reproduce our frontal

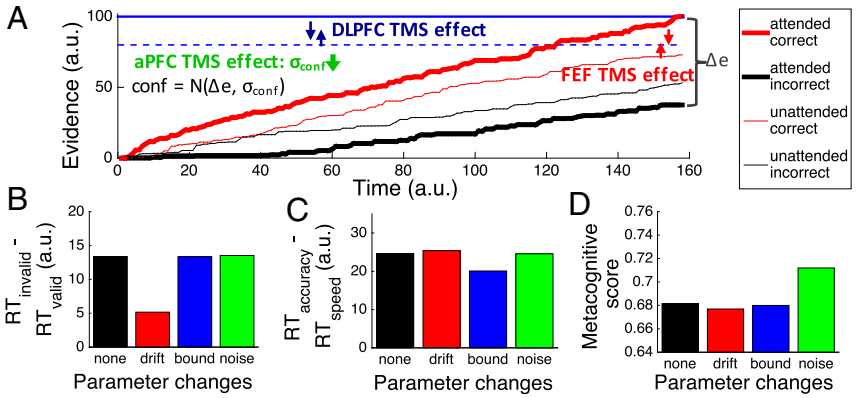

Fig. 3. Dynamic model of perceptual decision making. (*A*) Three critical parameters in our model were drift rate (the amount of perceptual evidence), bound (the decision criterion that controls how quickly subjects give their response), and confidence noise (the amount of noise added to the metacognitive decision). The figure depicts the evidence traces for an attended trial (thick lines) and an unattended trial (thin lines), as well as the decision criteria for accuracy focus (solid blue line) and speed focus (dashed blue line). The results of TMS to FEF, DLPFC, and aPFC were reproduced by changes in the difference between drift rates for attended and unattended stimuli (red arrows), the difference in the bound between the accuracy and speed instructions (blue arrows), and the confidence noise across all trials (green arrow), respectively. We performed four simulations runs changing each of these parameters, as well as a control simulation with default parameters. The predicted pattern of RT difference between unattended and attended stimuli (*B*), accuracy and speed instructions (*C*), and the metacognitive scores (*D*) was found, suggesting that TMS to different frontal brain regions affected different parameters within our dynamic decision model. a.u., arbitrary units.

TMS effects. First, the smaller difference in RT between attended and unattended targets after FEF TMS is reproduced by a smaller difference in the drift rate between attended and unattended conditions (red arrows in Fig. 3*A* and results in Fig. 3*B*). Second, the smaller difference in RT between accuracy and speed instructions after DLPFC TMS is reproduced by a smaller difference in the bound between speed and accuracy focus (blue arrows in Fig. 3*A* and results in Fig. 3*C*). Finally, the unexpected finding of higher metacognitive score after aPFC TMS is reproduced by a decrease in the confidence noise (Fig. 3*D*). Our simulations assumed that TMS to each of these regions affected only a single parameter of the model, which is why the simulated data do not perfectly reflect the empirical results (Fig. 2). For example, the metacognitive score after DLPFC TMS increased compared with our control site, but this increase is not reflected in the simulations. However, what is important here is the demonstration that the TMS effects on the processes of selection, criterion setting, and evaluation can be naturally understood computationally in the context of our model of dynamic decision making.

Frontal Organization Corroborated by fMRI. Our TMS results and model simulation were consistent with our predictions that progressively rostral frontal regions are involved in progressively later processing stages during perceptual decision making. Because, as we noted above, the three stages are temporally organized, another prediction is that more rostral frontal regions will become active later in the course of each trial of our task. We tested this prediction by using the fMRI data from day 2 to characterize the activity in frontal cortex during the (*i*) instruction, (*ii*) stimulus/perceptual judgment, and (*iii*) confidence epochs of the task. We do not claim that the selection, criterion setting, and evaluation processes occur exclusively during the instruction, stimulus/perceptual judgment, and confidence epochs of the task, respectively. Instead, a temporal hierarchy exists whereby the stimulus needs first be selected before decision criteria can be applied, and both of these processes need to occur before evaluation can take place. This temporal hierarchy implies that each process should peak later than the previous one, even in the absence of one-to-one correspondence between the three processes and the three task epochs. The design of our task was optimized for the TMS effects rather than this particular analysis, but the results confirmed our prediction nonetheless. Specifically, we found a clear rostrocaudal gradient such that the activity in progressively rostral frontal regions peaked during progressively later epochs of our task (Fig. 4).

We first examined the brain activity during each of the three epochs of the task (Fig. 4*A*). The whole-brain activation patterns for each task epoch are shown and discussed in greater detail in Fig. S1 (we note that the pattern of activity in the left hemisphere was similar to the right hemisphere, and we provide a link to complete unthresholded maps; *Materials and Methods*). Here, we focus on the results in the frontal cortex. We found that frontal cortex activity during the instruction epoch was mostly constrained to a caudal region, activity during the stimulus/perceptual judgment epoch extended from caudal to midlateral frontal regions, and activity during the confidence epoch extended across the entire lateral surface of the frontal cortex.

Critically, we found that progressively rostral frontal regions were activated maximally during progressively later task epochs (Fig. 4*B*). Indeed, we observed a significant interaction between region (FEF, DLPFC, aPFC) and task epoch (instruction, stimulus/perceptual judgment, confidence) [$F(4,40) = 22.16$, $P < 0.00001$, repeated measures ANOVA]. Specifically, FEF activity was greatest early in each trial, DLPFC activity was greatest in the middle of the trial, and aPFC activity was greatest at the end of the trial. The most caudal frontal region, FEF, was more active during the instruction [$t(20) = 2.09$, $P = 0.049$, d = 0.46] and stimulus/perceptual judgment [$t(20) = 4.31$, $P = 0.0003$, d = 0.94] epochs, compared with the confidence epoch. FEF activity during the instruction and stimulus/perceptual judgment epochs was not significantly different ($P = 0.99$), which may be explained by the observation that FEF is responsive to stimulus presentation (16). The middle frontal region, DLPFC, was more active during the stimulus/perceptual judgment epoch compared with both the instruction [$t(20) = 4.52$, $P = 0.0002$, d = 0.99] and confidence [$t(20) = 2.33$, $P = 0.03$, d = 0.51] epochs. Finally, the most rostral frontal region, aPFC, was less active during the instruction epoch compared with both the stimulus/perceptual judgment [$t(20) = 7.32$, $P = 4 * 10^{-7}$, d = 1.6] and confidence [$t(20) = 6.88$, $P = 1*10^{-6}$, d = 1.5] epochs. aPFC activations during the stimulus/perceptual judgment and confidence epochs were not significantly different ($P = 0.33$), which may be partly due to the evaluation process starting immediately after making the perceptual decision internally, which is likely a few hundred milliseconds before the

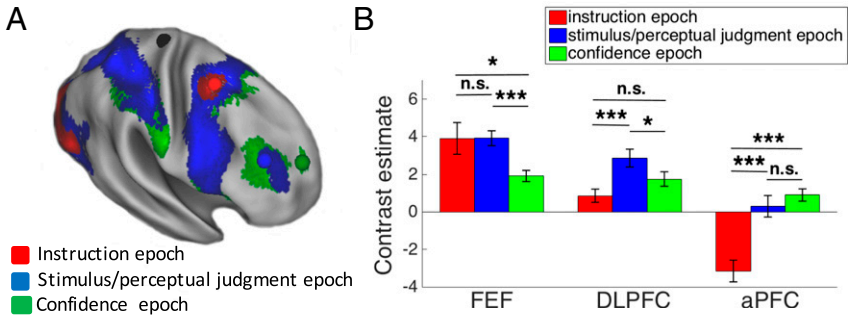

Fig. 4. fMRI results. (*A*) Brain activity corresponding to the instruction, stimulus/perceptual judgment, and confidence epochs. A caudal-to-rostral gradient is apparent with later epochs of the trial activating preferentially more rostral regions. The colored spheres are the mean locations of the stimulated S1 (black), FEF (red), DLPFC (blue), and aPFC (green) sites. (*B*) Mean blood-oxygenation-level–dependent (BOLD) contrast estimate for each trial epoch (beta value difference between the regressor for the relevant epoch and regressor for the "rest" period) is shown for each of the three regions, demonstrating that caudal regions are active earlier in the trial, whereas rostral regions are active later in the trial. Error bars represent SE. $*P < 0.05$; $***P < 0.001$.

button press that we used as an external indicator of the end of the stimulus/perceptual judgment epoch.

The above results were obtained by creating separate generalized linear model (GLM) models for each task epoch (*SI Materials and Methods*) to identify the full extent of activity during each task epoch. In a control analysis, we analyzed all three task epochs in the same GLM and obtained very similar results (Figs. S2 and S3).

Discussion

Despite numerous studies demonstrating the involvement of the frontal cortex in various high-level perceptual processes (2–5), the roles of distinct areas within frontal cortex during perceptual decision making remain underspecified. In this study, we provide a principle for frontal cortex functional organization based on the temporal organization of perception in the processes of selection, criterion setting, and evaluation. More specifically, convergent evidence from TMS and fMRI demonstrated that there are distinct frontal regions along a rostrocaudal (i.e., anterior-to-posterior) gradient that are necessary for the control of progressively later stages of the perceptual decision-making process.

Our results based on a causal intervention with TMS provide a critical addition to the literature on the contribution of frontal cortex to perceptual decision making that is largely based on correlational studies. Using correlational techniques, some studies claimed that relatively caudal regions of the frontal cortex are important for some of the later perceptual stages of processing. For example, speed/accuracy signals were found in FEF neurons (24), and confidence signals were found in supplementary eye field neurons (25). However, in our study, disruption of caudal frontal cortex function with TMS did not have a significant effect either on speed/accuracy or on confidence. It is possible that these differences are due to interspecies variation in the organization of frontal cortex and/or the substantial difference in the tasks used. Another important possibility is that because the perceptual decision was indicated via a saccade in both of these studies, the speed/accuracy and confidence signals were passed to the eye movement effector system but were nevertheless computed in more anterior areas of frontal cortex. This possibility is consistent with a recent study in which monkeys indicated the perceptual decisions using their hands and speed/accuracy signals were present in the primary motor cortex even though it is unlikely that these signals originated there (26). More studies that use causal interventions in both humans and monkeys are needed to determine the etiology of the discrepancies between our and these previous studies.

The functional gradient revealed in our data has strong implications regarding the general organization of the frontal cortex. A critical mass of studies has suggested the existence of a rostrocaudal gradient in the frontal cortex (1, 7–10). Although these studies differ in the details of the type of processes or representations being linked to each PFC subregion, each proposes a hierarchical organization with more rostral regions involved in the processing of more abstract representations (1, 7). Other studies, however, have proposed that the lateral frontal cortex is homogeneous in function without a functional gradient (12, 27, 28). This debate is complicated by the correlational nature of most previous studies. However, two previous studies of patients with focal brain lesions found causal support for a rostrocaudal gradient in frontal cortex (9, 10). The current results extend these previous patient studies by providing causal evidence from healthy human subjects in support of a rostrocaudal functional organization of frontal cortex.

Simulations based on a dynamic computational model of perceptual decision making (21–23) were able to reproduce the observed empirical TMS effects. The decrease in the RT advantage for attended stimuli following FEF TMS could be reproduced by decreasing the difference in drift rate between attended and unattended stimuli. Thus, one possibility is that the caudal frontal cortex biases the processing of visual information such that one stimulus is favored over another through a process akin to gain amplification (16, 29). This possibility is further corroborated by the known connectivity of FEF to early visual areas that respond to the visual stimulus (30). The decrease in the RT difference between accuracy and speed focus following DLPFC TMS could be reproduced by decreasing the difference in the decision bound between the two conditions. One possibility is that DLPFC is involved in the adjustment of the decision criterion. Such a role is facilitated by the wide connectivity of DLPFC with higher visual and parietal (as well as premotor and subcortical) areas (5). Finally, the improved metacognitive performance after aPFC TMS could be reproduced by decreasing the noise term in confidence decisions, consistent with a role of aPFC in metacognitive evaluations. This type of metacognitive process likely requires communication only with other high-level regions, such as frontal and parietal cortices, which is consistent with the connectivity pattern of aPFC (31). In summary, even though our simulations were intended as, and should only be seen as, a proof of concept, they are consistent with a rostrocaudal organization of frontal cortex function in relation to visual perception. A similar idea has been put forth in the context of linking perception with action (1).

Surprisingly, we found improvement in metacognition after aPFC TMS. Despite the unexpected nature of this result, it is actually in line with a pair of recent studies. The first one reported similar metacognitive enhancement after aPFC TMS on a memory task (32). The second one showed that monkeys with lesions to

rostral frontal cortex showed behavioral improvements on certain tasks (33). Specifically, they remained more focused in exploiting the current task when faced with various interruptions, potentially suggesting a role for rostral frontal cortex in reallocating cognitive resources for new purposes. Nevertheless, metacognitive impairment after TMS to a more posterior site in middle frontal gyrus has also been reported (34). Critically, in our study, average confidence ratings were not affected by aPFC TMS; instead, what was improved was the correspondence between the trial-by-trial confidence ratings and accuracy. Several types of explanations have been provided for TMS-induced performance improvements. For example, if TMS suppresses the noise more than the signal, behavioral performance would improve rather than decline (35). Another possibility is that behavioral performance can improve if TMS disrupts processes that are normally detrimental to the experimental task (36). This last explanation also fits with the monkey data discussed above (33). In partial support of this last possibility, we previously suggested a role for aPFC in decreasing the amount to which confidence on a previous trial biases the confidence rating on a current trial, a phenomenon dubbed "confidence leak" (37). Such confidence leak is likely beneficial in most everyday tasks but is suboptimal in laboratory tasks in which successive trials are independent and the previous stimulus should therefore be ignored during the current decision. Additional analyses (*SI Results*) demonstrated that aPFC TMS decreased the amount of confidence leak, which could have contributed to the improvements in metacognition. Nevertheless, in the absence of direct neural evidence, each of these explanations remains speculative. Regardless of the explanation of our finding, it does support a critical role for aPFC in metacognition, and is consistent with the existence of a rostrocaudal gradient in frontal cortex for perception.

Materials and Methods

Forty-one subjects were tested in an initial screening session. Twenty-one of these subjects were able to perform the task appropriately by following both the attentional and speed/accuracy instructions, and were therefore invited to participate in the five additional days of testing. Four subjects were unable to complete all six sessions; thus, a total of 17 subjects completed the study (11 females and 6 males, average age = 23.06 y, age range: 21–30 y). All participants had normal or corrected-to-normal vision. They received detailed information about the potential side effects of TMS and provided written informed consent. All procedures were approved by the University of California, Berkeley Committee for the Protection of Human Subjects.

All behavioral data and codes that reproduce every analysis and figure are freely available at https://github.com/DobyRahnev/TBS-to-PFC. In addition, unthresholded fMRI maps are uploaded at neurovault.org/collections/599.

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