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Distinct neural mechanisms of distractor suppression in the frontal and parietal lobe

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The posterior parietal cortex and the prefrontal cortex are associated with eye movements and visual attention, but their specific contributions are poorly understood. We compared the dorsolateral prefrontal cortex (dlPFC) and the lateral intraparietal area (LIP) in monkeys using a memory saccade task in which a salient distractor flashed at a variable timing and location during the memory delay. We found that the two areas had similar responses to target selection, but made distinct contributions to distractor suppression. Distractor responses were more strongly suppressed and more closely correlated with performance in the dlPFC relative to LIP. Moreover, reversible inactivation of the dlPFC produced much larger increases in distractibility than inactivation of LIP. These findings suggest that LIP and dlPFC mediate different aspects of selective attention. Although both areas can contribute to the perceptual selection of salient information, the dlPFC has a decisive influence on whether and how attended stimulus is linked with actions.

To cope effectively with complex environments, organisms must be able to select relevant information and keep it online until it is linked with action. Achieving this goal requires balancing the demands of top-down and bottom-up (task and stimulus related) factors, a balance that is governed by systems of working memory and selective attention[1–7].

Neurophysiological studies in monkeys have identified an interconnected network of frontal and parietal areas that is particularly important for target selection and eye movement control, and includes LIP, the frontal eye field (FEF) and the dlPFC[8–12]. Neurons in all three areas have spatially tuned activity that selects targets relative to distractors in a variety of tasks[9–11], and their experimental manipulation (through microstimulation or reversible inactivation) affects visual orienting through covert attention and overt saccades[13–18] as well as neural activity in the remaining centers[9,19]. Thus, the LIP, FEF and dlPFC seem to make joint contributions to spatial working memory and visual attention.

A key question raised by these investigations concerns the specific contribution of each node in this network. Two recent studies compared responses to target selection during efficient (pop-out) and inefficient (conjunction) visual search, but produced inconclusive results. The first study reported that the latency of neural selection for a pop-out target was shorter in LIP (see also ref. 20) relative to FEF and the dlPFC, whereas the opposite was true for conjunction search[21]. A subsequent study, however, failed to replicate this result, and instead found that dlPFC cells had early selection latencies that were comparable with those in LIP[22]. Thus, the specific contributions of the LIP, FEF and dlPFC remain poorly understood.

A common aspect of these comparative investigations is that, even though they compared efficient and inefficient search, they invariably focused on target selection. Thus, the studies do not establish whether the frontal and the parietal lobes make distinct contributions to top-down versus bottom-up selection, defined as orienting to task-relevant targets versus irrelevant distractors. LIP neurons were shown to encode both target selection and rapid transient shifts of attention to irrelevant flashed distractors[23,24], but these attention shifts remained covert and did not trigger overt actions. This suggests that the brain may have dissociable mechanisms that select stimuli for perception or action, but the neural substrates of these mechanisms are not fully known.

To address this question, we compared the LIP and dlPFC using a memory-guided saccade task in which a salient, but task-irrelevant, distractor was flashed at various timings and locations during the memory delay. We found that, although LIP neurons had robust responses to both targets and irrelevant distractors, dlPFC cells much more strongly suppressed irrelevant distractors. Distractor suppression in the dlPFC was stronger and acted on longer temporal and spatial scales; moreover, it was anticipatory and curtained the early visual response, distinguishing it from previously described forms of motor inhibition. Consistent with these neural results, reversible inactivation of the dlPFC produced much stronger increases in distractibility than inactivation of LIP. Our results suggest that the LIP and dlPFC are specialized for different aspects of attention control. Although both areas can guide selection for perception, the dlPFC has a privileged role in determining whether or how stimuli gain access to actions.

RESULTS

Behavior

Two monkeys performed a modified version of an oculomotor memory task in which they were presented with a 100-ms flash of a peripheral target and, after a 1,600-ms delay period, made an eye

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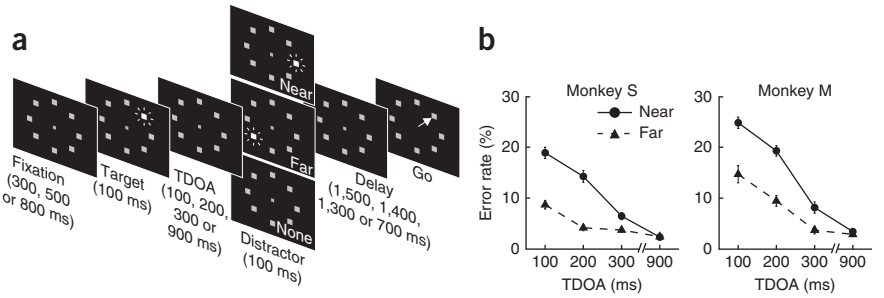

Figure 1 Task and behavioral performance. (**a**) Task stages are shown with time running from left to right. An array of eight placeholders remained continuously on the screen, and a trial began with a variable period of central fixation. This was followed by a 100-ms flash indicating the target location. After a variable TDOA, a distractor flashed after target presentation. The distractor was identical to the target in appearance and duration, but appeared at either a near-target location (angular separation of 45°) or far locations (separations 135° or 180°). One third of trials (randomly interleaved) were no-distractor trials. After an additional delay (bringing the total delay period to 1,600 ms) the fixation point disappeared (Go) and monkeys were rewarded for making a saccade to the target location. (**b**) Performance for each monkey as a function of distractor distance and TDOA (mean and s.e. across all recording sessions, $n = 89$ sessions in monkey S, 47 sessions in monkey M).

movement to the remembered target location (**Fig. 1a**). On two-thirds of the trials, a 100-ms distractor was flashed during the delay interval at a randomly selected target-distractor onset asynchrony (TDOA) of 100, 200, 300 or 900 ms. In addition, the distractor location was randomly selected to be near (45° angular separation) or far from the target location (135 or 180° separation). All trial conditions (distractor present or absent, TDOA and distance) were randomly interleaved in a block. The target and distractor were identical in appearance and duration, so that monkeys had to remember the location of the first stimulus and suppress the subsequent distractor.

Both monkeys had near perfect performance if the distractor appeared at a late (900 ms) TDOA at near or far locations (**Fig. 1b**), consistent with previous reports[24,25]. However, errors became increasingly more common as distractors became more similar to the target in both time and space. A two-way ANOVA on the error rates revealed significant effects of distance and TDOA, and a significant interaction, such that the largest fraction of errors was found for near-target, short TDOA distractors (all $P < 0.001$, for combined data and each monkey individually). Error saccades were virtually always directed to the distractor location and only rarely directed to unmarked locations in the display (<3% of trials), and this error pattern remained stable over the course of data collection. Thus, the monkeys' errors were not the results of visual masking or incomplete understanding of the task, but instead reflected the power of a distractor to interfere with the target-related saccade.

dlPFC shows weaker distractor responses relative to LIP

To understand the neural mechanisms mediating the distractor interference, we collected data from 77 spatially tuned neurons in the dlPFC (51 in monkey S, 26 in monkey M) and 59 neurons in LIP (38 in monkey S, 21 in monkey M). All of the neurons selected had spatial receptive fields as determined by preliminary testing with the memory-guided saccade task (see Online Methods). During the distractor task, the placeholder array was scaled and rotated so that one placeholder fell in the estimated center of a cell's receptive field. Thus, on different trials, the target, the distractor or neither stimulus fell onto the central receptive field location.

LIP and dlPFC neurons had similar responses to the task-relevant target on correct trials (**Fig. 2**). These responses included a large transient visual response followed by a lower-level delay period activity that exceeded the response to non-target locations, consistent with previous observations[9,10,26,27]. Despite this similar response to target selection, the two areas had markedly different responses to the salient distractors (**Fig. 2**). In LIP, the distractor responses were weaker than those evoked by the target (one-way ANOVA followed by *post hoc* paired tests, $P < 0.001$ for each distractor distance and TDOA, in each area, in both the combined data and individually in each monkey). However, distractor responses were still robust enough to transiently surpass the sustained response at the target location. In the dlPFC, in contrast, distractors barely evoked a response, even though they appeared in the receptive field center. In the following analyses, we first measured the peak responses elicited by the distractors and their correlation with performance. We then describe two distinct components of distractor suppression that acted, respectively, on firing rates prior to distractor onset and on the distractor-evoked visual response.

Peak distractor responses in the dlPFC reflect behavior

For each distractor distance and TDOA, the peak responses evoked by the distractor were significantly weaker in the dlPFC relative to LIP (one-way ANOVA followed by *post hoc* tests, $P < 0.001$ for each comparison). These differences were consistent both in the entire sample (**Figs. 2** and **3a**) and in each monkey (**Supplementary Fig. 1**), and remained robust when we examined the raw (not normalized) firing rates.

In addition to having weaker distractor responses, dlPFC showed a spatio-temporal profile that was more closely correlated with the monkeys' performance relative to that in LIP (**Fig. 3a**). Similar to the monkeys' error rates, distractor responses in the dlPFC were highest for distractors that were close to the target in space and time (two-way ANOVA, $P < 0.001$ for main effects of distance, TDO and interaction, in the combined data and each monkey individually; **Figs. 1b** and **3a**). Across the different conditions, the distractor responses in the dlPFC were positively correlated with the monkeys' error rates ($r = 0.31$, $P < 0.001$; monkey S, $r = 0.931$, $P = 0.001$; monkey M, $r = 0.562$, $P = 0.147$; **Fig. 3b**). In LIP, however, there was no such correlation ($r = 0.0435$, $P = 0.325$; $P = 0.405$ for monkey S, $P = 0.960$ for monkey M; **Fig. 3b**). Notably, the LIP cells had equivalent or stronger responses to the far relative to near distractors ($P < 0.01$ for 100-ms TDOA; **Fig. 3a**), even though the far distractors triggered far fewer inappropriate saccades (**Fig. 1b**).

To gain additional insight into the mechanisms leading to an error, we analyzed the time at which the neurons reported the monkeys' decision. We compared activity preceding correct and error saccades, focusing on trials with near distractors at 100-ms TDOA, which provided the greatest number of errors. To determine the time course of modulation of the target and distractor response, we separately analyzed the trials in which the distractor or the target was in the receptive field (**Fig. 4**).

Activity in both areas reflected the monkeys' saccades regardless of the stimulus configuration (**Fig. 4**). Activity was higher if the saccade was directed to the receptive field center rather than to the adjacent

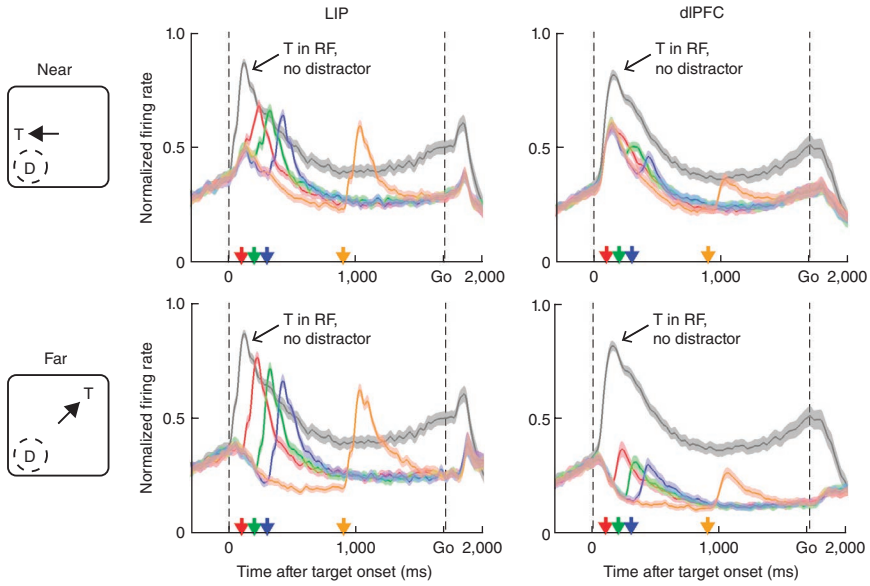

Figure 2 Neural responses in LIP and dlPFC. Average normalized firing rates in each area aligned on the onset of the target and Go signal (0 and 1,600 ms). The gray traces show trials in which the target (T) was in the receptive field (RF) and no distractor appeared. The colored traces show trials in which a distractor (D) appeared in the receptive field at 100-, 200-, 300- or 900-ms TDOA (red, green, blue and orange arrows and traces, respectively). Raw firing rates were smoothed by convolving with a Gaussian kernel (15 ms s.d.). Firing rates were normalized by dividing each neurons' activity by its peak target response (T in receptive field, no-distractor) and the normalized traces were averaged to obtain the population response. Shading shows s.e.m. As shown in the cartoons, distractor trials were sorted according to whether the target had appeared near the receptive field (top row) or far from the receptive field (bottom row).

location, whether that saccade was made correctly or in error. The latency of this neural discrimination, however, differed by area and configuration, and was shortest for the distractor response in the dlPFC. When a distractor was in the receptive field, dlPFC neurons showed an enhancement on an error relative to a correct trial at 259 ms after distractor onset (**Fig. 4**). The same cells, however, showed suppression of the target-related response only at a longer latency (306 ms after distractor onset; **Fig. 4**). The corresponding neural events were also reflected in LIP, but with a longer time course, that is, 324 ms for enhancement of the distractor response and 430 ms for suppression of the target response (**Fig. 4**). The neurons also showed slight differences in their baseline firing rates during the fixation epoch before stimulus presentation (time 0; **Fig. 4**), which may reflect fluctuations in covert attention, motivation or anticipation during the fixation period. These differences, however, were weak and statistically significant only when the target, but not a distractor, was in the receptive field ($P < 0.05$). Notably, the differences were no longer visible during the peak visual response ($P > 0.1$ for in each area and condition), suggesting that they did not directly explain the neurons' discrimination of saccade direction. Thus, the earliest consistent predictor of the monkeys' choice was a failure of distractor suppression in the dlPFC; this was followed at longer latencies by reduction of the target-related response in the dlPFC and, finally, by the corresponding events in LIP.

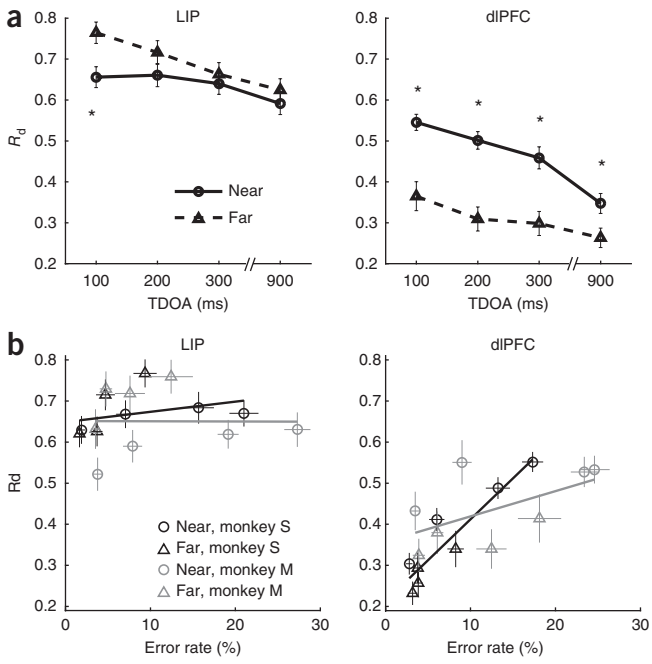

Figure 3 Correspondence between distractor responses and error rates. (**a**) The peak-normalized response to the distractor (mean ± s.e.m.) as a function of distance and TDOA. Asterisks indicate significant difference between near and far distractors (paired *t* test, $P < 0.001$). (**b**) The correlation between distractor responses and error rates. Each point shows the fraction of errors and distractor response (mean ± s.e.m.) for a different monkey, distance and TDOA.

Distinct components of distractor suppression

A closer inspection of the peak distractor response suggests that it was shaped by two mechanisms. The first mechanism was a gradual decrease in firing that developed before the appearance of the distractor itself (**Fig. 2**). The second mechanism was a modulation of the additional response evoked by the distractor that was independent of the pre-existing rates.

To quantitatively analyze the pre-distractor (anticipatory) suppression, we selected trials with 900-ms TDOA and far-target distractors, which showed the strongest effect (**Fig. 5a**). Focusing on the pre-distractor response, we fitted the target-aligned firing rates with an exponential decay function, $R(t)=R_1e^{(-t\tau)}$, where R is the raw (not normalized) firing rate, t is time (0–500 ms after target onset), R_1 is the baseline firing rate (in a 50-ms window centered on target onset) and τ is a fitted time constant. The time constant τ was significantly higher in the dlPFC (9.11, 95% confidence intervals of [8.7629, 9.4613]) relative to LIP (7.13, [6.6663, 7.5941]), indicating that response suppression was faster in the former area.

Although anticipatory suppression was strong at far separations, it was less apparent at near-target locations (**Fig. 2**). A two-way ANOVA with distance and area as factors (800–900 ms after target onset, 900-ms TDOA) revealed that pre-distractor responses were lower at far relative to near separations ($P < 0.001$ for main effect of distance; $P < 0.005$ in each monkey). Moreover, there was a significant area by distance interaction, such that the responses at far, but not at near,

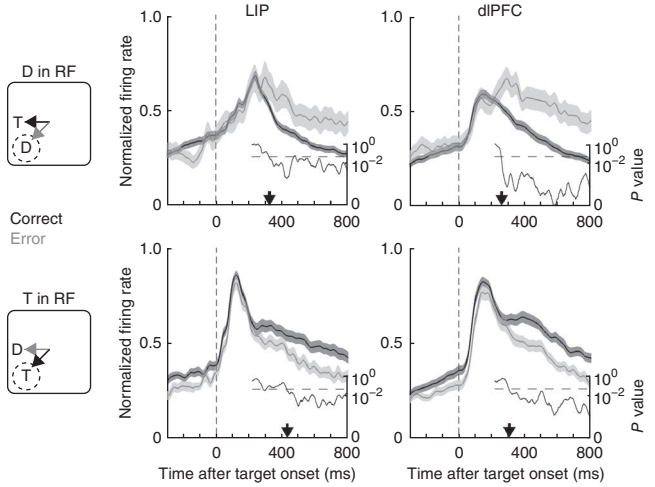

Figure 4 Analysis of error trials. Population responses preceding correct saccades (dark gray) and error saccades (light gray) on trials with a near distractor at 100-ms TDOA. After an initial visual response, neural activity became stronger whenever the saccade was directed to the receptive field center. When a distractor was in the receptive field (top), activity was stronger for an error relative to a correct saccade (top). When a target was in the receptive field (bottom), activity was stronger for a correct relative to an error trial. The red trace and axes (log scale) show the *P* values resulting from a sliding window *t* test comparing correct and error trials (window width = 1 ms, step size = 1 ms). The dashed lines show the $P = 0.05$ significance level and the black arrows on the *x* axis show the time of consistent discrimination (when the *P* values remained consistently below 0.05).

separations were weaker in the dlPFC ($P < 0.05$ for effect of area in combined data and in each monkey individually). In the near condition, neurons had a small response to the target (**Fig. 2**) as a result of the fact that the target fell within the receptive field border for a majority of cells (the target response was significantly higher than the pre-target baseline ($P < 0.05$) in 67 of 77 neurons in the dlPFC and 44 of 59 neurons in LIP). However, the level of this target-related response was not correlated with the neurons' anticipatory pre-distractor activity (LIP, $r = 0.009$, $P = 0.952$; dlPFC, $r = 0.201$, $P = 0.103$; **Fig. 5b**), suggesting that receptive field overlap was not the primary reason for the weak near-target suppression. In sum, anticipatory suppression was strongest at far relative to near-target separations, and was stronger and developed more quickly in the dlPFC than in the LIP.

We next examined the additional response evoked by the distractor above and beyond the pre-existing rates. To quantitatively measure this response, we calculated for each cell the difference between its spike density histograms on distractor and no-distractor trials (**Fig. 5c**). We then found the peak of this difference histogram and measured firing rates in a 100-ms window centered on this peak. Finally, we normalized this maximum response by dividing by the peak target response minus the pre-target baseline (the latter measured in the 100-ms window centered on target onset). This quantity, which we refer to as ΔR_d, measures the additional response that is evoked by a distractor relative to the additional response evoked by the target, factoring out the pre-existing rates.

ΔR_d showed a spatio-temporal profile that differed from that of the pre-distractor response (**Fig. 5c**). Although the pre-distractor firing was most strongly suppressed at far separations, ΔR_d was most strongly suppressed at near-target locations. Moreover, ΔR_d tended to increase with time at near separations, even as the pre-distractor firing gradually declined (**Fig. 2**). A two-way ANOVA on ΔR_d revealed that the effect of distance was significant in both the dlPFC and LIP (each $P < 0.001$). A significant effect of TDOA and a TDOA × distance interaction were found in LIP (both $P = 0.005$), showing that, at near separations, ΔR_d increased significantly as a function of TDOA. In the dlPFC, however, there was no effect of TDOA or distance by TDOA interaction (both $P > 0.05$), indicating that ΔR_d remained low in all conditions.

These findings suggest that ΔR_d is controlled independently of the pre-distractor rates and is influenced by two mechanisms. A transient suppression at near separations (100–200 ms) was found in both areas and seems similar to the visual adaptation reported in other structures[28]. In the dlPFC, however, ΔR_d remained low even outside the range of adaptation (far separations and long TDOAs), suggesting that it is affected by additional mechanisms that act on longer timescales.

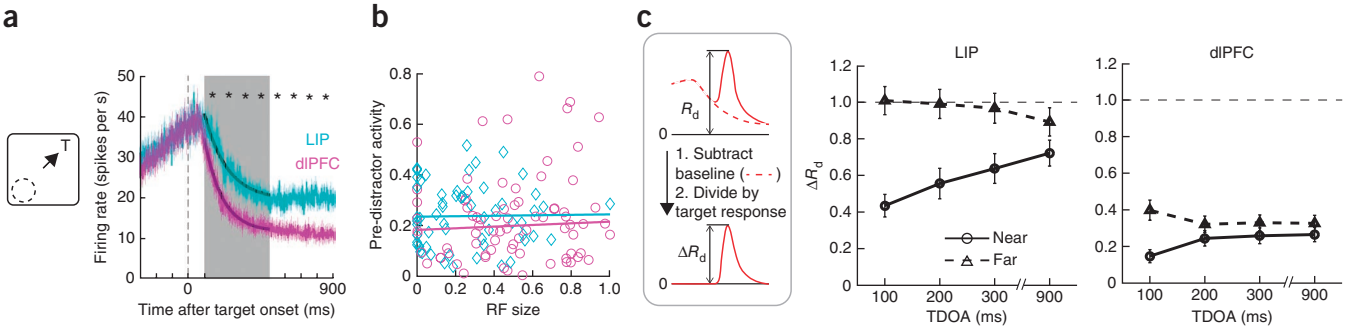

Figure 5 Anticipatory and visual suppression. (**a**) Pre-distractor responses in LIP and dlPFC on trials in which the target appeared opposite the receptive field and a distractor appeared at 900-ms TDOA (distractor responses not shown). Histograms show unsmoothed firing rates measured in 2-ms time bins. Black traces show the exponential fit of firing in the 100–500-ms interval indicated by shading. Asterisks denote 100-ms non-overlapping bins in which firing rates differed significantly between LIP and dlPFC ($P < 0.05$). (**b**) Pre-distractor responses for near separations were unrelated to receptive field size. Each point shows the average pre-distractor activity of one neuron for near distractors (800–900 ms after target onset, 900-ms TDOA) as a function of the neuron's receptive field size. Receptive field size was defined as the ratio of the magnitude of response to the target presented 45° away from the center of receptive field and in the receptive field center. Thus, values close to 1 indicate a wide receptive field with equivalent responses at the center and adjacent location, whereas values close to 0 indicate a smaller receptive field. The lines are best-fit linear regressions. Although receptive field sizes were larger in the dlPFC relative to LIP ($P < 0.05$), they were not consistently related to the pre-distractor response in either area. (**c**) Visual distractor responses (mean ± s.e.m. across all neurons), computed as shown on the left. For each distance and TDOA, the additional distractor response (ΔR_d) in dlPFC was significantly smaller than that in LIP (all $P < 0.001$).

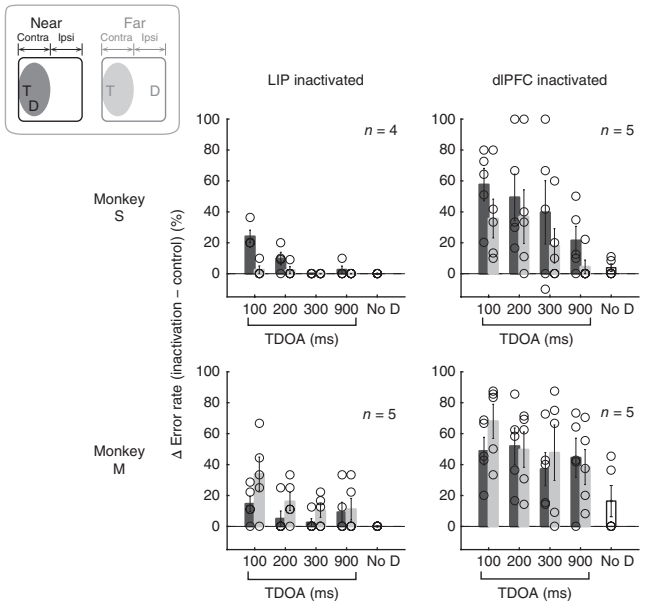

Figure 6 Effects of reversible inactivation of LIP and dlPFC. As shown in the cartoon at the top left, the target was in the hemifield contralateral to the inactivation site (shading) in these trials and was accompanied by either a near distractor (dark gray) or a far distractor (light gray). In the data panels, each circle indicates the difference in error rate between a single inactivation and control session. The bars show the average ± s.e.m. In both monkeys for all TDOAs and distances, dlPFC inactivation induced more errors than LIP inactivation. The deficits were larger on trials that did, relative to those that did not, contain a distractor (no D, white bars).

Reversible inactivation

As an additional test of each area's role in distractor suppression, we examined the effects of local reversible inactivation using the GABA-A receptor agonist muscimol[15,16]. At the end of neural recording sessions we infused muscimol (5 mg ml^{-1}) at locations at which we had previously recorded neurons. A volume of 1 µl of muscimol was injected at ten sites in the dlPFC (five in monkey M), and volumes of 3 or 8 µl were injected at nine sites in LIP (four in monkey M). Control performance was recorded on interleaved days without inactivation.

In trials in which the target was in the hemifield contralateral to the inactivation site (**Fig. 6**), inactivation of the dlPFC produced a marked increase in the errors in each behavioral session ($P < 0.001$ in each condition). The increase in error rates was larger on distractor than on no-distractor trials ($P = 0.002$; monkey S, $P = 0.050$; monkey M, $P = 0.014$), suggesting that inactivation impaired the ability to suppress distractors rather than merely remember the target location. If a distractor appeared, the inactivation effects were similar across distractor conditions (two-way ANOVA, effect of TDOA, $P = 0.069$ in monkey S, $P = 0.479$ in monkey M; effects of distance and interaction, all $P > 0.05$), consistent with the broad range of neural suppression. In addition to increasing the rate of distractor-directed saccades, dlPFC inactivation produced an increase in the frequency of fixation breaks both before and after target presentation (one-way ANOVA inactivation versus control, $P < 0.05$ for monkey S, $P < 0.001$ for monkey M; **Supplementary Fig. 2**).

Inactivation of LIP (**Fig. 6**) produced significant increases in error rates if the target was in the contralateral field ($P < 0.001$ overall; monkey S, $P = 0.003$; monkey M, $P < 0.001$), confirming previous observations[13–15]. These deficits, however, were much milder relative to those obtained in the dlPFC (one-way ANOVA, $P < 0.001$ for effect of area in each monkey; **Fig. 6**). This result could not be explained by injection size, as larger muscimol amounts were consistently injected in LIP (3–8 µl) relative to dlPFC (1 µl). In addition, monkey S, who received only the larger 8-µl injections, tended to show milder behavioral deficits than monkey M, who received both 3- and 8-µl injections ($P < 0.07$ for effect of monkey). As for the dlPFC, LIP inactivation produced no errors on no-distractor trials. However, in contrast with the dlPFC, the increase in error rates after LIP inactivation did reveal a small dependence on timing, such that larger deficits occurred at short TDOAs (two-way ANOVA for distance and TDOA, $P < 0.001$ for monkey S, $P < 0.05$ for monkey M for main effect of TDOA), with an inconsistent dependence on distance (monkey S, larger effects for far, $P < 0.001$; monkey M, larger effects for near, $P < 0.05$). Also in contrast with the dlPFC, LIP inactivation did not affect the number of fixation breaks (all $P > 0.05$; **Supplementary Fig. 2**). These findings suggest that LIP has a relatively minor contribution to distractor suppression, which tends to be restricted to short TDOAs.

Consistent with the neurons' contralateral receptive field, inactivation did not impair performance on trials in which the target was ipsilateral to the inactivated hemisphere (**Supplementary Fig. 3**). In monkey S, a significant improvement in performance was seen after both dlPFC and LIP inactivation (dlPFC, $P < 0.001$; LIP, $P = 0.046$), although this was not seen in monkey M (dlPFC, $P = 0.91$; LIP, $P = 0.41$).

DISCUSSION

Despite the similarity of their responses to target selection, the LIP and dlPFC make vastly different contributions to distractor suppression. Distractor responses were weaker and more tightly correlated with performance in the dlPFC than in the LIP. Consistent with these findings, reversible inactivation of the dlPFC produced much greater impairment in distractor suppression than did inactivation of LIP.

Relation with motor inhibition

Although our results implicate the dlPFC in distractor suppression, the type of suppression that we described differs markedly from previously reported motor mechanisms. In studies of saccade inhibition, monkeys are trained to execute a saccade on the majority of trials, and, on a small proportion, must unexpectedly cancel this preplanned saccade. One mechanism that allows saccade inhibition relies on neurons in the substantia nigra, superior colliculus and the frontal lobes, which are tonically active during stationary fixation, and can inhibit saccade movement cells[29–31]. A second mechanism involves so-called 'don't look' cells, which have been described in the pre-supplementary motor area[32] and at prefrontal sites more posterior to the ones that we investigated[33], which have spatially selective, transient responses for a cancelled or re-directed saccade.

Both these mechanisms differ from the present observations because they rely on a strong excitatory response that can actively inhibit motor mechanisms. In contrast, we found that dlPFC cells had only very weak distractor responses, and these responses were weakest when the distractor was successfully suppressed (on correct relative to error trials). Similarly, reversible inactivation of an inhibitory mechanism is expected to elevate error rates by reducing the inhibitory drive at the distractor location[32]. In the dlPFC, however, inactivating the distractor location had a beneficial, rather than impairing, effect (**Supplementary Fig. 3**).

Our results therefore reflect a distinct form of suppression that, rather than inhibiting remote structures, operates in the dlPFC. This form of suppression does not rely on an active 'break' that inhibits

a donwstream saccade motor plan; instead, it involves anticipatory suppression and strong inhibition of the visual distractor response.

Distinct roles in saccades and attention

The manipulations that we used, the planning of a memory-guided saccade and an abrupt onset distractor, are powerful attentional cues[34,35] and it is likely that, in addition to saccade planning, our task recruited perceptual attention. Consistent with this interpretation, LIP neurons did show the expected attentional effects, including a relative enhancement of the target relative to the distractor responses, and a modest deficit following reversible inactivation[13–15]. Thus, following a previous study that used a similar task, we suggest that covert attention was allocated to the target location throughout most of the delay period, but transiently shifted to the distractor location for the brief period in which distractor responses were high in LIP[23,24].

Previous investigations have also implicated frontal areas in attention[18,36], and our findings are consistent with such an influence. Our findings suggest that such top-down effects are mediated primarily by enhancement of activity at the target location, with distractor suppression arising indirectly through local competition. This conclusion is consistent with the recent anatomical finding that frontal projections to posterior areas terminate overwhelmingly onto excitatory (spiny) cells[37] and with normalization models of selective attention[38]. It is important to note that the attentional influences documented by previous research were mediated by the FEF rather than the dlPFC[18,36]. Thus, whether the role of the dlPFC may be direct or mediated by an indirect pathway through the FEF remains an important question for future investigation.

Most notably, however, our results indicate that, even though both areas may be involved in perceptual attention, the dlPFC has a privileged role in linking stimuli with actions. Relative to LIP, dlPFC responses much more closely reflected the monkeys' error pattern, and its inactivation much more strongly affected the monkeys' ability to suppress inappropriate saccades. Thus, the dlPFC and LIP seem to have distinct roles in selective attention. Although both frontal and parietal areas may contribute to the selection of stimuli for covert (perceptual) processing, the frontal lobe has a special role in identifying action-relevant information. This distinction between attention for perception and attention for action is reminiscent of the dichotomy between 'attention for learning' and 'attention for action' proposed in studies of associative learning in humans and rats[39].

Implications for attractor models and local circuitry

The very different spatio-temporal properties of the distractor responses that we have observed also suggest that the LIP and dlPFC have important differences in their local circuitries. A leading computational model of spatial working memory is based on attractor networks, which generate persistent activity by virtue of local recurrent excitation balanced by global inhibition to remote neuronal pools[40]. Our findings are consistent with the idea that an attractor architecture is implemented in the dlPFC, but not in LIP.

One important prediction of an attractor architecture is a similarity effect, whereby distractors that are more similar to the target generate stronger interference because they activate overlapping, and thus more weakly suppressed, neural populations[41]. Here we found a behavioral similarity effect, such that the largest fraction of errors was triggered by distractors that were more similar to the target in space as well as time. This proximity effect was reflected in the peak responses in the dlPFC, which were strongest for near distractors at short TDOAs (**Fig. 3a**), but it was not encoded in LIP, where neurons tended to respond more for far relative to near distractors (**Fig. 3a**).

A second feature of an attractor network is its critical dependence on distractor suppression for protecting an existing memory trace. In attractor networks, a bottom-up input that is insufficiently suppressed will force a transition to a new attractor state[42,43]. Consistent with this prediction, a failure of distractor suppression in the dlPFC was the earliest event predicting an error (**Fig. 4**). In stark contrast with this pattern, LIP neurons maintained their target-evoked responses even while responding strongly to the salient distractor. This phenomenon had been noted previously for target and distractor locations that were well separated in opposite hemifields[24,25,44], and here we found that it generalizes to near-target locations. One possibility is that LIP implements an attractor network, but uses a different gating mechanism for governing the transition from transient to sustained activity. This seems unlikely, however, as inactivation of LIP had only a weak effect on behavioral distractibility, suggesting that its sustained target-related response was not critical for correct performance. A more parsimonious interpretation is that LIP does not generate sustained activity through an attractor mechanism, but derives its sustained response through feedback from the frontal lobe[44].

Finally, consistent with the long-range inhibition required by an attractor regime, our findings indicate that the dlPFC implements several inhibitory mechanisms that act on longer spatial and temporal scales. One such mechanism was an anticipatory reduction in the neurons' firing rates that was strongest at far relative to near-target locations, and was stronger in the dlPFC relative to LIP. A wholesale suppression of the neurons' spiking output may be produced by parvalbumin-reactive basket cells that form extensive terminal plexi on the cell bodies of pyramidal cells and can curtail the entire spiking output at remote locations[45,46].

The second mechanism produced a more specific reduction in the additional distractor response (ΔR_d; **Fig. 5c**). This input-specific suppression had a local, transient component that reduced ΔR_d at near-target locations at short TDOA, and acted in both LIP and in the dlPFC. This form of suppression seems consistent with cell-intrinsic adaptation, which has been proposed previously for the superior colliculus and the FEF[28,47] and may be ubiquitous throughout visual areas. In the dlPFC, however, ΔR_d remained low even at long TDOAs and near-target locations, that is, outside of the temporal window of adaptation and of the spatial range of anticipatory suppression. This suggests that an additional form of suppression acts specifically on a visual input and is stronger in the dlPFC. This mechanism may be mediated by inhibitory synapses on pyramidal dendrites from calbindin-positive interneurons or somatostatin-expressing Martinotti cells[45,48,49].

METHODS

Methods and any associated references are available in the online version of the paper.

Note: Supplementary information is available in the online version of the paper.

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AUTHOR CONTRIBUTIONS

M.S. and J.G. conceived the experiment. M.S. collected and analyzed the data. J.G. wrote the manuscript.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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ONLINE METHODS

Behavioral and neurophysiological methods. Two adult male rhesus monkeys (*Macaca mulatta*) weighing 8–10 kg were tested with standard behavioral and neurophysiological techniques as described previously[50]. All methods were approved by the Animal Care and Use Committees of Columbia University and New York State Psychiatric Institute as complying with the guidelines in the Public Health Service Guide for the Care and Use of Laboratory Animals. Data were analyzed offline using Matlab (MathWorks). Visual stimuli were displayed on an MS3400V XGA high-definition monitor (62.5 × 46.5 cm viewing area; CTX International) located 57 cm in front of the monkeys' eyes. The time of all visual transients was measured by means of a photodiode mounted on the screen that indicated the onset of a vertical refresh.

Electrode tracks were aimed based on stereotactic coordinates and structural magnetic resonance imaging. For LIP, tracks were aimed to the lateral bank of the intraparietal sulcus and for the dlPFC, they targeted the posterior portion of the principal sulcus just anterior to the pre-arcuate region from which saccades are elicited with low-threshold microstimulation (FEF)[51]. Neurons were tested further if they had spatially tuned activity on a standard memory-guided saccade task[52]. *Post hoc* testing revealed that all neurons had spatial tuning during the visual epoch and the vast majority maintained this tuning during the memory delay (800–1,200 ms after target onset, 33 of 46 neurons in LIP, 68 of 77 in dlPFC, $P < 0.05$, one-way ANOVA for spatial tuning).

Reversible inactivation. Muscimol injections were targeted to recording coordinates that yielded reliable visuospatial tuning during the recording sessions in both dlPFC and LIP (in the right hemisphere in monkey M and left hemisphere in monkey S). Muscimol (Sigma) was dissolved in phosphate-buffered saline, pH~7, to concentrations of 5.0 mg ml^{-1}, and immediately before an experiment, was backfilled into a 10-µl Hamilton syringe (Recording Micro Syringe MRM-S02, Crist Instruments). To limit damage to neural tissue, we performed a single needle track in each experiment and infused muscimol at a single depth along the track. When possible, we confirmed the presence of spatially tuned activity before injection and the silencing of this activity after the injection by multi-unit recording through an electrode attached to the Hamilton syringe. Infusion depths ranged between 2 and 6 mm (mean ± s.d., 3.8 ± 1.1 mm) below the cortical surface. To avoid pressure damage, injections were made in small steps of 0.5 µl at 2–3-min intervals. The total volume injected was 1 µl for dlPFC and between 3 and 8 µl for LIP, corresponding to a total amount of 5 µg of muscimol for dlPFC and 15–40 µg for LIP. Behavioral testing was completed within 2.5 h of the muscimol infusion. Control data were obtained on alternate days without inactivation, using precisely the same tasks, presentation order and parameters as during the inactivation session. During four injections of physiological saline (one in each area in each monkey), we found no difference between no-injection and post-injection data, indicating that the effects could not be explained by nonspecific tissue damage produced by injection pressure.

Data analysis. To measure distractor responses (**Figs. 2** and **3**), firing rates were smoothed with a Gaussian filter (15 ms s.d.) and normalized for each cell by dividing by the peak target–evoked response (T in receptive field, no-distractor). Because individual cells showed consistent visual latencies (as can be appreciated in the sharp onset of the population response), we measured visual responses in a 100-ms time window that remained constant across cells. In one analysis method, we centered the window on the latency of the peak population response to the target (**Fig. 2**) and at the corresponding latency for each distractor TDOA. In a second method, we centered the window on the peak distractor response for each TDOA. These methods yielded equivalent findings, and, for simplicity, only the former is reported in the text. Baseline firing rates were measured in a 100-ms window centered on the target onset, except when computing ΔR_d, when we subtracted the neural response on no-distractor trials as described for **Figure 5c**.

Because different cells were tested with far distractors that had either a 135° or a 180° angular separation, we could further examine whether suppression differed when the target and distractor were in the same or in opposite hemifields. We separated neurons into three distinct classes: neurons tested with same-hemifield 135° distractors ($n = 19$ in LIP, 25 in dlPFC), opposite-hemifield 135° distractors ($n = 20$ in LIP, 25 in dlPFC) and 180° distractors (all opposite hemifield; $n = 20$ in LIP, 24 in dlPFC). We found no significant difference of these distractor conditions in any area or monkey and for any TDOA (all $P > 0.1$), suggesting that the suppression of remote distractors was equivalent within and across the different hemifields.

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