Systems/Circuits

Inactivation of Parietal Reach Region Affects Reaching But Not Saccade Choices in Internally Guided Decisions

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The posterior parietal cortex (PPC) has traditionally been considered important for awareness, spatial perception, and attention. However, recent findings provide evidence that the PPC also encodes information important for making decisions. These findings have initiated a running argument of whether the PPC is critically involved in decision making. To examine this issue, we reversibly inactivated the parietal reach region (PRR), the area of the PPC that is specialized for reaching movements, while two monkeys performed a memory-guided reaching or saccade task. The task included choices between two equally rewarded targets presented simultaneously in opposite visual fields. Free-choice trials were interleaved with instructed trials, in which a single cue presented in the peripheral visual field defined the reach and saccade target unequivocally. We found that PRR inactivation led to a strong reduction of contralesional choices, but only for reaches. On the other hand, saccade choices were not affected by PRR inactivation. Importantly, reaching and saccade movements to single instructed targets remained largely intact. These results cannot be explained as an effector-nonspecific deficit in spatial attention or awareness, since the temporary "lesion" had an impact only on reach choices. Hence, the PPR is a part of a network for reach decisions and not just reach planning.

Key words: internally guided decisions; parietal reach region; posterior parietal cortex; reaching; saccades; spatial extinction

Significance Statement

There has been an ongoing debate on whether the posterior parietal cortex (PPC) represents only spatial awareness, perception, and attention or whether it is also involved in decision making for actions. In this study we explore whether the parietal reach region (PRR), the region of the PPC that is specialized for reaches, is involved in the decision process. We inactivated the PRR while two monkeys performed reach and saccade choices between two targets presented simultaneously in both hemifields. We found that inactivation affected only the reach choices, while leaving saccade choices intact. These results cannot be explained as a deficit in attention, since the temporary lesion affected only the reach choices. Thus, PRR is a part of a network for making reach decisions.

Introduction

In high-pressure situations, such as driving on a highway, people have limited time to make decisions. How do we decide which action is the best to follow at any given time? A long-established view suggests that decision making is a distinct cognitive process from perception and action in value-based decisions (Tversky and Kahneman, 1981; Padoa-Schioppa and Assad, 2006; Padoa-Schioppa, 2011). According to this theory, neuronal ensembles in frontal brain areas represent the value of the alternative options (Roesch and Olson, 2004; O'Doherty, 2011; Padoa-Schioppa and Cai, 2011). This representation is abstract in the sense that the value of each option is computed by integrating decision variables into a subjective value, without taking into account the sensorimotor contingencies of the choice. The subjective values are compared and the best option is selected. Critically, action planning begins only when a decision is made.

While this goods-based theory is sufficient to explain abstract value-based decisions, like trading in the stock market, recent studies argue against this theory for decisions that involve immediate physical actions. According to these studies, decisions between actions emerge via a competition between neuronal populations within the same brain areas that plan actions (Glimcher et al., 2005; Cisek, 2007, 2012; Cisek and Kalaska, 2010;

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Rangel and Hare, 2010). Support for this model includes the formation of potential actions before decisions (Cisek and Kalaska, 2005; Cui and Andersen, 2007) and the coding of decision variables, such as expected reward by sensorimotor regions (Platt and Glimcher, 1999; Pastor-Bernier and Cisek, 2011). However, it has been argued that these findings are not related to the decision process, but rather to spatial attention (Gottlieb et al., 1998; Bisley and Goldberg, 2003; Leathers and Olson, 2012).

These findings create considerable uncertainty regarding whether brain regions that have traditionally been associated with planning actions are also part of the decision process. One way to establish whether particular regions are involved in the decision process is to temporarily perturb these regions through pharmacological inactivation and observe the effects on decision making. Studies in monkeys have shown that unilateral lateral intraparietal (LIP) area inactivation leads to a reduction of contralesional choices in oculomotor decisions (Wardak et al., 2002; Balan and Gottlieb, 2009; Wilke et al., 2012). Similar effects were found in saccade choices (Wilke et al., 2013) and in reach and grasp choices (Wilke et al., 2010) by inactivating subcortical regions, such as the pulvinar, as well as in visual search and reach target-selection tasks after inactivating the superior colliculus (McPeek and Keller, 2004; Song et al., 2011).

Despite the contribution of these studies to our understanding of the functional role of particular brain regions, they do not distinguish whether the choice bias after inactivation is due to a bias in decision making or a bias in attention. For instance, the neglect-like symptoms observed in monkeys after pulvinar inactivation could be related either to attentional deficits or deficits in the decision process (e.g., devaluation of the contralesional hemifield; Wilke et al., 2010). To address this question, we need to explore whether the choice bias is effector specific. In the current study, we explored the role of the parietal reach region (PRR) in internally guided decisions—i.e., free choices that are not informed by any external contingencies. The PRR is located in the medial bank of the intraparietal sulcus (IPS) and is specialized for reaches (Gnadt and Andersen, 1988; Snyder et al., 1997). We tested the hypothesis that PRR inactivation alters the selection between two equally rewarded options exclusively for reaches. We reversibly inactivated the PRR while two monkeys performed memory-guided reach or saccade movements to either a single target or one selected from two targets presented simultaneously in both hemifields. Consistent with our hypothesis, we found that PRR inactivation led to a strong reduction of contralesional reach choices without affecting the saccade choices. Hence, the choice bias after PRR inactivation is effector specific, indicating that PRR is causally involved in reach decisions.

Materials and Methods

Surgery

Two adult male rhesus macaques (*Macaca mulatta*) weighing 10–12 kg were implanted with a MRI-compatible polyether etherketone head holder and two bilateral Ultem chambers (16 mm inner diameter) over the IPS. All surgical and animal care procedures were done in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the California Institute of Technology Institutional Animal Care and Use Committee.

Inactivation procedure

Microinfusions of the $GABA_A$ agonist muscimol (Tocris Bioscience) were made in each inactivation session using a stainless-steel beveled-tip cannula (30 gauge; Plastics One). The cannula, affixed to a custom holder driven by a microdrive (FHC, Inc.), was lowered in each inactivation session to the injection site. The muscimol was dissolved in PBS and the solution, pH 7.0–7.45, was sterile filtered (Corning) before injection. Total injection volumes ranged from 5.5 to 6.5 μl and were delivered at a rate of 1.0 μl/min using a 100 μl gas-tight Hamilton syringe driven by a digital infusion pump (Harvard Apparatus). The infusions were performed while the animals were awake and sitting in a primate chair, with their heads restrained via implanted head posts. All the injections were performed in the right PRR in animal G (left handed) and in the left PRR in animal H (right handed). The behavioral experiment started ~15–20 min after finishing the injection and lasted up to 2 h.

Structural MRI acquisition

To identify the site of injections, anatomical MR images of the animals were acquired in a Bruker Biospec 4.7 T, 60 cm vertical monkey bore scanner equipped with a BGA38S2 gradient coil. The animals were well adapted to the scanner environment and sat awake in a primate MR-compatible chair (Kagan et al., 2010). Scans were performed using a custom-made quadrature surface RF coil (H. Merkle), surrounding the back and the side portions of the animals' heads. Coronal anatomical T1-weighted images were acquired using a modified driven equilibrium Fourier transform sequence with an in-plane resolution of 0.5 mm and a slice thickness of 0.8 mm.

Behavioral tasks

Memory-guided reaches. The animals sat in a dark room ~30 cm from an LCD monitor, in an upright position in an enclosed primate chair, with a two-dimensional (2D) joystick positioned between their legs. A reaching trial started with the "initial fixation" period, in which two central fixation spots were presented in the center of the screen. The animals had to fixate one spot (red diamond) and to acquire the other one (green circle) by moving a cursor (size 0.3 cm) controlled by the joystick (Fig. 1*A*). If the animals moved the cursor outside the green circle (7.5 cm diameter) or broke eye fixation (i.e., moved their gaze outside a window of 7.5 cm, corresponding to 14° of visual angle) during the "initial fixation" period, the trial was aborted. After 1 s, either a single green cue (instructed trial) or two green cues (free-choice trial) were presented for 300 ms, indicating the location of the target(s). Both types of trials were randomly interleaved in each session. The two cues were presented simultaneously in both the left and right hemifield, equidistantly from the central fixation points. In the free-choice trial, one cue was presented in a specific location in one of the visual fields, and the other at the mirror-image location in the opposite visual field. The cues were randomly selected from 12 locations (18–30° eccentricity, six in the right and six in the left visual field).

Following the cue offset, the animals were required to memorize the position of the cues and maintain both eye and hand fixation for 2–4 s for monkey G and 1.5–2.5 s for monkey H. We used a shorter memory delay period for monkey H because his reaching performance decreased with longer memory delays. When the green central fixation spot was extinguished ("go signal"), the animals had to perform a correct reach by moving the cursor to the instructed or to the chosen remembered target location without breaking central eye fixation. The size of the target was 7.5 cm (corresponding to a diameter of 14°). The animals had to wait for another 300 ms to receive the reward on successful trials. The animals were rewarded with water only if a trial was successful—i.e., the reaching movement was made to the instructed target or to one of the two choice targets. The actual location of the target was reilluminated for both correct and incorrect trials. Both animals used the arm opposite to the inactivated hemisphere for reaching. They also received the same amount of reward during the free-choice trials as during the instructed trials and were rewarded equally for selecting either target in the free-choice trials. Any trial in which the animals broke eye fixation or moved their hand before the go signal was aborted. Only successful trials were used for further analysis.

Memory-guided saccades. The saccade task was similar to the reach task with the main difference being that the location of the target(s) was indicated by a red diamond cue with side length of 1.5 cm (Fig. 1*B*). A saccade trial started with a red diamond fixation spot presented in the center of the screen. After 1 s, either a single red cue (instructed trials) or

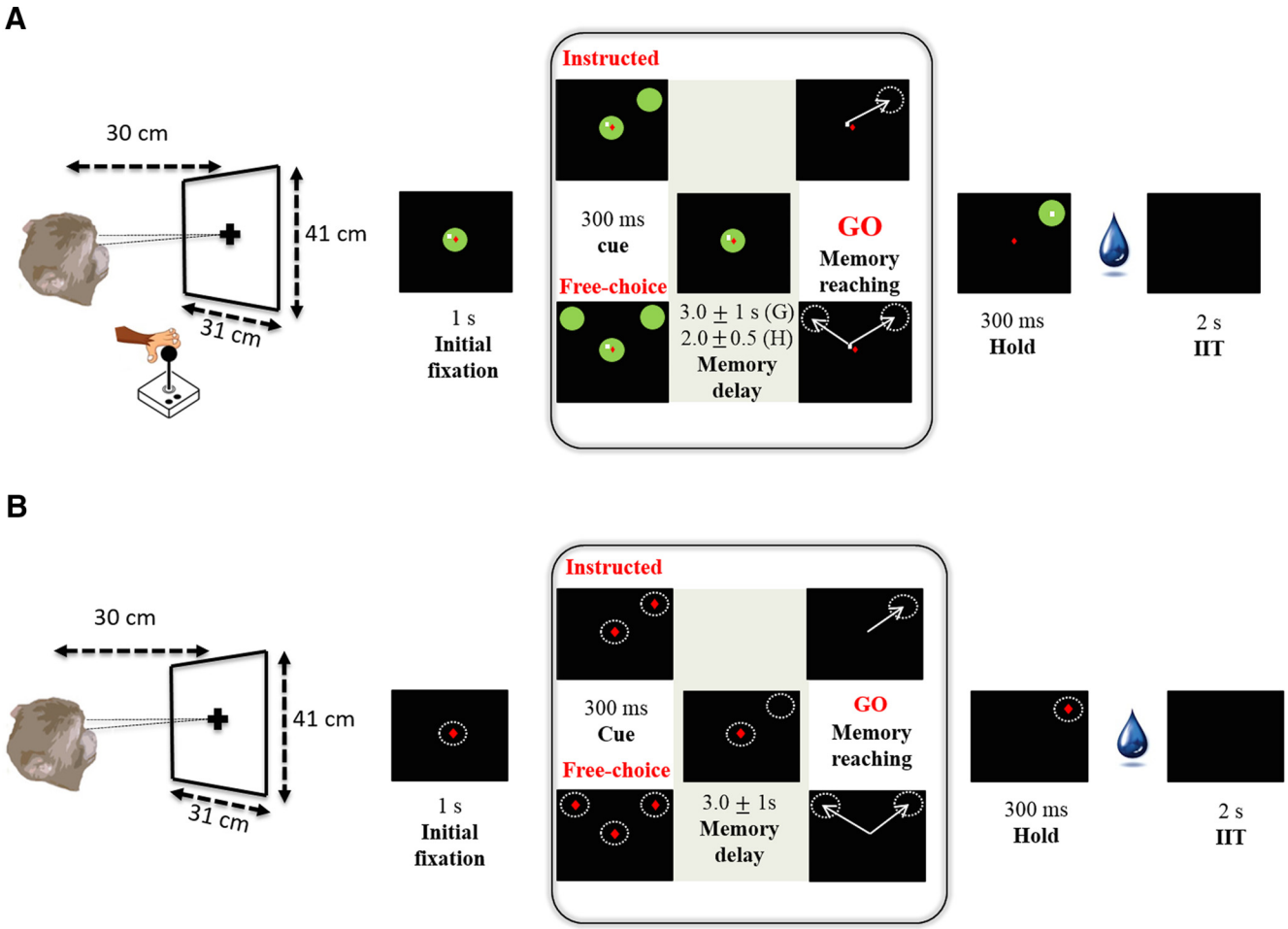

Figure 1. ***A***, Memory-guided reaching task. The animals sat in an upright position in an enclosed primate chair, with a 2D joystick positioned between their legs. The joystick was used for reaches, as it allows for both imaging and task performance within an MRI scanner in future experiments. Appearance of two central fixation spots began the trial and the animals acquired one spot (red diamond) with the eyes and the other one (green circle) with the joystick. Next, either a single target was presented in the left or right visual field (instructed trials) or two targets were presented simultaneously to both fields (free-choice trials). The targets were randomly selected from 12 locations (18–30° eccentricity, 6 in the right and 6 in the left visual field). Then, the targets disappeared for a delay period and, after the go signal (green central fixation spot was extinguished), the animals made a movement to the instructed or chosen target. The target was then reilluminated for feedback and the animals were rewarded with water only if the trial was successful—i.e., a movement was made to the instructed target or to one of the two choice targets. Eye fixation was required during the reach trials. Note that we used a shorter memory delay period for monkey H because his reaching performance decreased for longer memory delays. ***B***, Memory-guided saccade task. The memory-guided saccade task was similar to the memory-guided reaching task with the difference that the animals performed saccades to either a single target or one selected from two targets presented simultaneously in both hemifields. Red diamond cues indicate the location of the targets.

two red cues (free-choice trials) were presented for 300 ms, indicating the location of the target. The cues were randomly selected from the same 12 locations used in the reaching task. The animals had to memorize the position of the target(s) for 2–4 s. After the central fixation cue was extinguished (i.e., go signal), the animals had to perform a memory-guided saccade to the single target or to the chosen target. If the eyes arrived at the target within a tolerance of 7.5 cm (corresponding to a window diameter of 14°), the target was reilluminated and the animals had to maintain fixation for another 300 ms before receiving the reward. The large window diameter was chosen for compatibility with reaching trials. Successful saccade trials were rewarded with the same amount of water that the animals received in the successful reaching trials. Trials in which the animals broke eye fixation before the go signal were aborted and were not used for further analysis. Note that the animals were not required to maintain hand fixation during saccade trials; the cursor representing the joystick position was not shown.

Behavioral data analysis. We measured the reaction time (RT) and the movement time (MT) of the reaches both in the instructed and the free-choice trials. RT was defined as the time at which the reach velocity first exceeded 5% of the peak reach velocity. MT was defined as the time between the go signal and the movement offset (i.e., the time that the hand velocity first dropped below 5% of the peak reach velocity after the time that the peak velocity was detected on each trial). We also measured the reaching and saccade performance of the animals by computing the proportion of correctly executed reaches and saccades, respectively, in instructed trials. Finally, we computed the proportion of choices to the contralesional and ipsilesional hemifield in the free-choice trials. The proportion of choices was computed using only correct reach and saccade trials. Originally, we performed the analysis separately for each single target and every pair of targets in the instructed and free-choice trials, respectively, to explore whether the consequences of PRR inactivation depend on target locations. We found no systematic effect of PRR inactivation on particular target locations within a given hemifield. This lack of effect is likely due to the fact that the targets were large and were placed only above the horizontal center of the screen. We did not use targets in the lower quadrants after we found a significant drop in reaching performance in initial experiments because the animals had to move the joystick toward their body to reach lower targets. Because of this experimental set-up, there was a significant overlap between the targets, which may explain the lack of effect of PRR inactivation on particular target locations. In the following analysis, we therefore focused only on the differences between contralesional and ipsilesional targets regardless of their actual location within a hemifield.

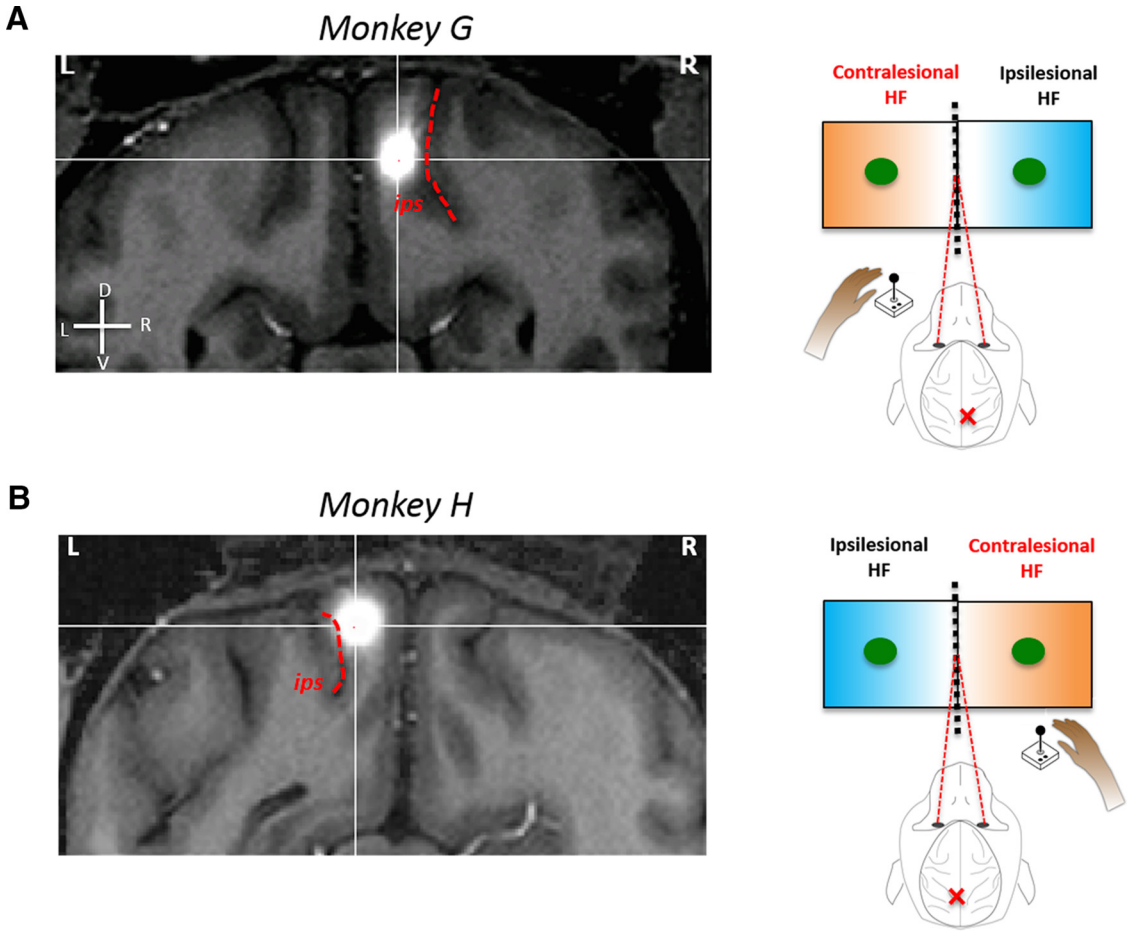

Figure 2. ***A***, Left, Coronal T1-weighted MR sections visualizing the injection sites for monkey G with gadolinium MR contrast agent (white). The injection image was acquired 15–30 min after 5.5 μl infusion. Right, We inactivated the right PRR, because monkey G was left handed. Hence, the left hemifield is the contralesional side and the right hemifield is the ipsilesional side for monkey G. ***B***, Left, Similar to ***A***, but for monkey H. Right, We inactivated the left PRR of monkey H because he was right handed. Therefore, the left and the right hemifields are the ipsilesional and contralesional sides, respectively, for monkey H.

Stimulus presentation, online control, and data acquisition. Visual stimuli were presented via an LCD monitor using custom Python software based on PsychoPy (Peirce, 2008). Eye position was monitored at 60 Hz with a miniature infrared camera (Resonance Technology), using ViewPoint software (Arrington Research). Reaching movements were performed using a 2D joystick (Measurement Systems). The position of the joystick was monitored at the same frequency as the eye position. Both eye and joystick positions were recorded simultaneously with the stimulus and timing information. Online behavioral control and feedback were implemented in Python.

Results

We tested the consequences of PRR inactivation on internally guided decisions by performing local injections of the $GABA_A$ agonist muscimol while two monkeys performed memory-guided reach (Fig. 1*A*) or saccade movements (Fig. 1*B*) to a single target (instructed trials) or one selected from two targets presented simultaneously in both hemifields (free-choice trials). Injection sites were localized by injecting the MRI-visible contrast agent gadolinium, which is known to correspond closely to the spread of muscimol (Heiss et al., 2010), and imaging its spread with MRI using a 4.7 T vertical bore scanner (Wilke et al., 2012). The spread of the gadolinium showed that the inactivation was performed primarily within a restricted volume of the medial bank of the IPS, corresponding to PRR (Fig. 2*A*, for monkey G; Fig. 2*B*, for monkey H). Monkey G performed six control sessions (i.e., no PRR inactivation) involving both reach and saccade trials, and four control sessions involving only the reach task. In the inactivation sessions, monkey G performed four sessions of the reach task only, and four sessions that involved both the reach and saccade tasks. Similarly, monkey H performed seven control sessions involving both the reach and saccade tasks, and three control sessions that involved only the reach task. This monkey performed six inactivation sessions involving both the reach and saccade tasks and one session with only the reach task (Table 1 summarizes the number of control and inactivation sessions for each animal). Per session, monkey G performed 430 ± 63 (mean ± SEM) and 484 ± 46 trials in the control and inactivation reaching task, respectively. This monkey did 293 ± 51 and 289 ± 63 trials per session in the control and inactivation saccade task. Monkey H performed 372 ± 24 trials and 381 ± 30 trials per session in the control and inactivation reaching task. This monkey did 248 ± 28 and 237 ± 22 trials per session in the control and

Table 1. The number of control and inactivation sessions performed by the animals

Control sessions		Inactivation sessions	
Monkey G	Monkey H	Monkey G	Monkey H
6 reaches + saccades 4 reaches only	7 reaches + saccades 3 reaches only	4 reaches + saccades 4 reaches only	6 reaches + saccades 1 reach only

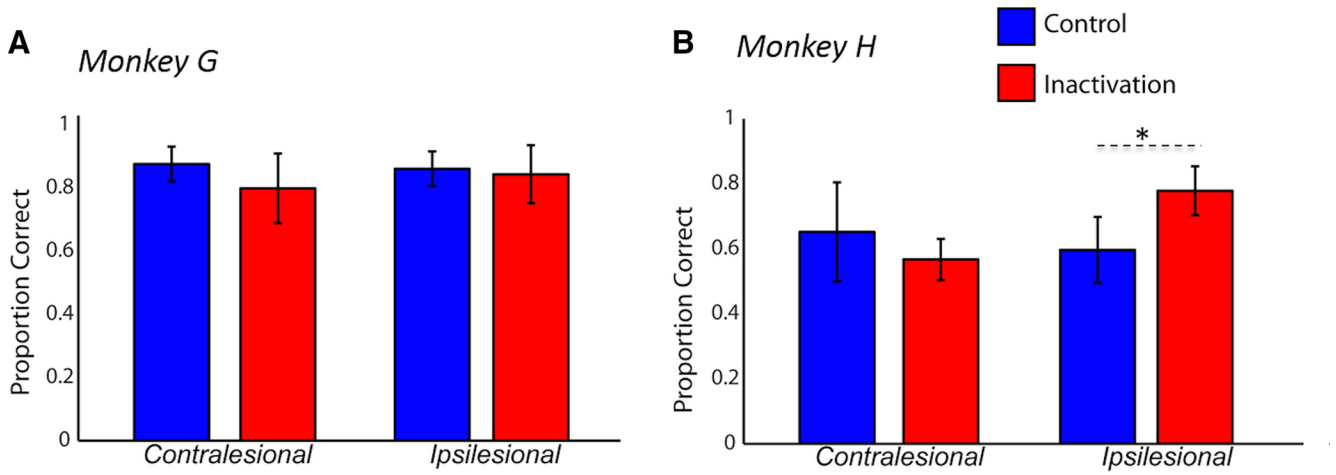

Figure 3. Proportion of correct reaches to instructed targets in the ipsilesional or contralesional hemifield during control and inactivation sessions for monkey G (***A***) and monkey H (***B***). Notice that inactivation did not impair the reaching performance of the animals. The only effect was the improvement of the reaching performance for monkey H for reaches to the ipsilesional hemifield. The error bars indicate SD across all sessions (10 and 8 control and inactivation sessions, respectively for monkey G, and 10 and 7 control and inactivation sessions, respectively, for monkey H). *$p < 0.01$.

inactivation saccade task. Control sessions were interleaved with muscimol injection sessions with a minimum interval of 24 h. To minimize the potential risks from repeated injections (e.g., bleeding, infection) and stress to the monkeys, control sessions did not include saline injections. The animals used the arm opposite to the inactivated hemisphere for reaching movements. Throughout the paper, the terms "ipsilesional" and "contralesional" refer to the visual hemifield with respect to the inactivated hemisphere. Particularly, monkey G used the left hand to perform reaches and for this reason we injected the drug into the right PRR. In this case, the contralesional side was the left hemifield and the ipsilesional side was the right hemifield (Fig. 2*A*). In contrast, monkey H used the right hand in reach trials and hence we injected the drug into the left PRR. In this case, the left hemifield was the ipsilesional side and the right hemifield was the contralesional side (Fig. 2*B*).

Inactivation effects on memory reaches—instructed trials

To examine the effects of PRR inactivation on reaches toward memorized targets, we used a delayed memory reaching task with single targets presented in either the left or right visual field. Figure 3*A*,*B* depicts the reaching performance (i.e., proportion of correct trials) before and after PRR inactivation for monkey G (*A*) and monkey H (*B*). The results showed that drug injection did not impair the ability to perform memory reaching movements to instructed single targets in the contralesional hemifield (two-tailed *t* test across sessions, $p > 0.05$). Also, we found that PRR inactivation did not affect the reaching performance for targets located in the ipsilesional hemifield for monkey G (two-tailed *t* test across sessions, $p > 0.05$). Interestingly, the ipsilesional reaching performance of monkey H was improved after drug injection (two-tailed *t* test across sessions $p < 0.01$). A potential explanation is that the performance of this animal was improved for reaches to the ipsilesional hemifield because he started selecting the ipsilesional targets more often in the free-choice trials after PRR inactivation, resulting in more practice in reaching to these targets. We also tested whether the PRR inactivation affected the temporal characteristics of reaching trajectories in the instructed trials. Figure 4*A* illustrates the average RT (i.e., departure time from the hand fixation after the go signal) for instructed trials for reaches to the contralesional and ipsilesional target before and after PRR inactivation. The results showed that muscimol injection did not cause any significant changes in RT in addition to a slight decrease of RT for ipsilesional reaches for monkey G (two-tailed *t* test across sessions, $p < 0.01$). Similarly, we found that PRR inactivation did not affect the MT of the instructed reaches (i.e., time between departing from the hand fixation and arriving at the goal; Fig. 5*A*; two-way ANOVA, hemifield × inactivation, $p > 0.05$). We should point out that whether or not PRR inactivation affects the temporal characteristics of reaching movements is still debated in the literature. For instance, our findings are in accord with the results from a recent study in our laboratory showing that PRR inactivation did not significantly affect the RT and MT in natural reaching movements to peripheral targets (Hwang et al., 2012). On the other hand, a similar study showed that PRR inactivation slowed the RT for reaches performed with the contralesional limb by 6.8 ms (Yttri et al., 2014). It is important to mention that a direct comparison between our findings and the results from these previous studies is not straightforward, since reaches in our experiment were performed using a 2D joystick. Overall, the lack of strong effects from muscimol injection on the reaching performance, as well as on the RT and MT of the reaches suggest that PRR inactivation did not cause any significant changes in the sensory, memory, and motor components of the task in the instructed trials.

Inactivation effects on memory reaches—free-choice trials

The next step was to evaluate whether muscimol injection affects the selection between two response options presented simultaneously in both hemifields. To this end, we used a delayed memory reaching task with two targets presented simultaneously in both the left and right visual field. Choosing either of the two targets provided the same amount of reward. Figure 6*A*,*B* depicts the proportion of choices to contralesional targets in control sessions and after drug injection for monkey G (*A*) and monkey H (*B*). The injections produced a strong reduction of contralesional choices. Particularly, in the control sessions, the animals more often chose the targets contralateral to the injection hemisphere (perhaps due to a lower biomechanical effort of reaching into the space nearer to the arm used Cos et al., 2011). In other words, monkey G used his left arm and initially preferred the left hemifield, while monkey H used his right arm and initially preferred

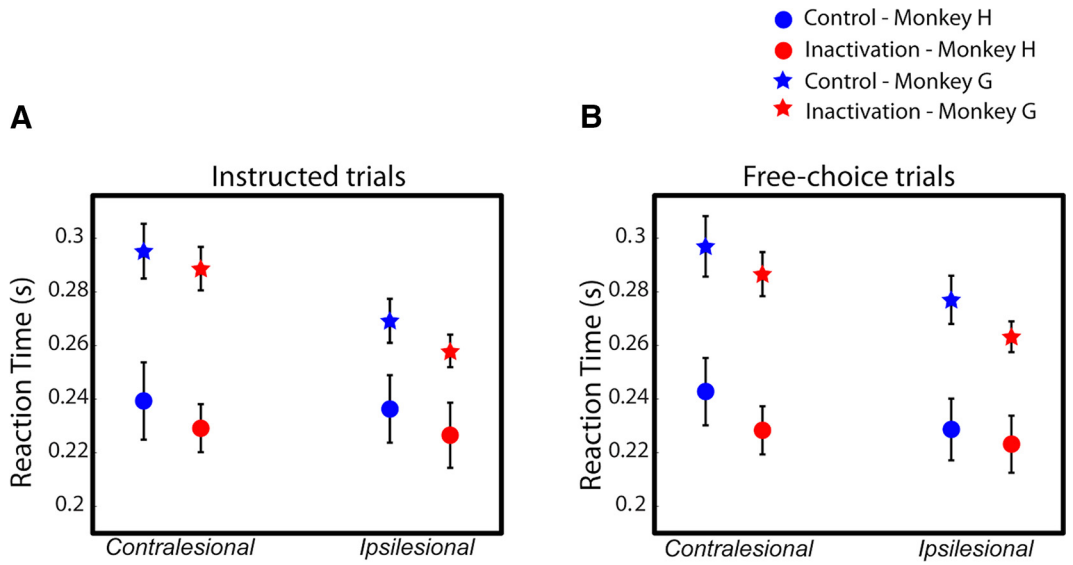

Figure 4. ***A***, Mean RT of correct reaching movements in the instructed trials during control and inactivation sessions. PRR inactivation did not cause any significant changes in the RT beside a slight decrease of the RT in ipsilesional reaches for monkey G. ***B***, Similar to ***A*** but for the free-choice trials. There were no significant changes in the RT in addition to a slight decrease of the RT in ipsilesional reaches for monkey G. The error bars indicate SD across all sessions (10 and 8 control and inactivation sessions, respectively, for monkey G, and 10 and 7 control and inactivation sessions, respectively, for monkey H).

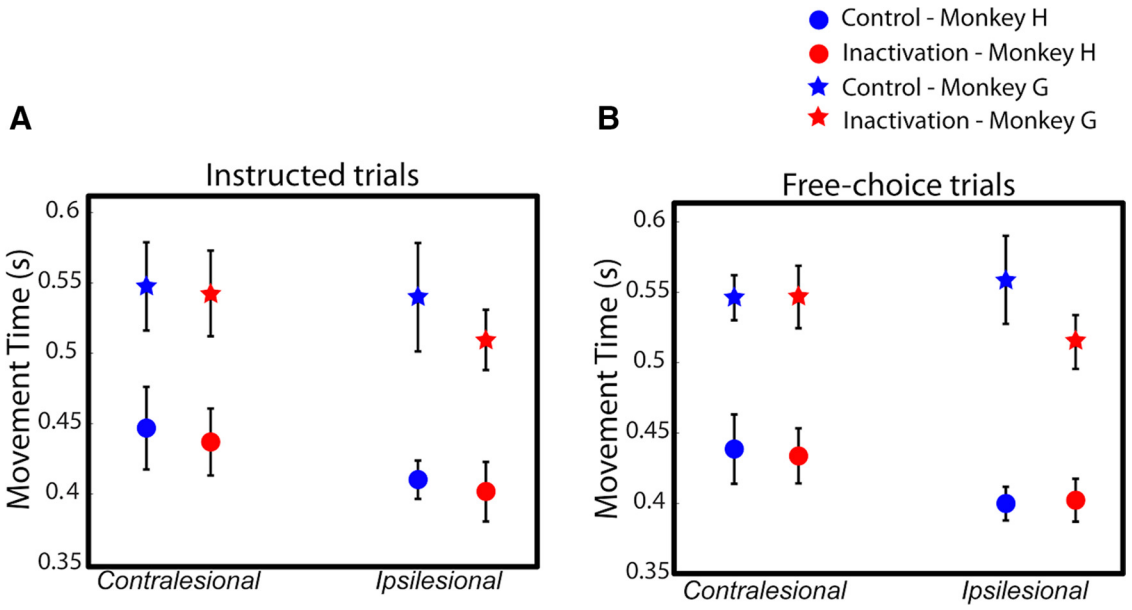

Figure 5. ***A***, Mean MT of correct reaches in the instructed trials during the control and inactivation sessions. The drug injection did not cause any significant changes in the MT. ***B***, Similar to ***A***, but for the free-choice trials. In this case, we found a slight decrease of the MT in ipsilesional reaches for monkey G. The error bars indicate SD across all sessions (10 and 8 control and inactivation sessions, respectively, for monkey G, and 10 and 7 control and inactivation sessions, respectively, for monkey H).

the right hemifield. However, in the inactivation sessions, the choice bias flipped to a preference for targets on the ipsilesional side (two-tailed t test across sessions, $p < 10^{-6}$). Similar to the instructed trials, we found that drug injection did not affect the temporal characteristics of the reaches, such as the RT and MT, in the free-choice trials, except for a slight decrease of the RT and MT for reaches to the ipsilesional targets for monkey G (two-tailed t test across sessions, $p < 0.01$; Figs. 4*B*, 5*B*). Hence, PRR inactivation caused a profound choice bias to the ipsilesional targets, leaving the sensory, memory, and motor components of the task in the free-choice trials largely intact.

Finally, we tested whether the choice bias was diminished over the course of repeated injections, due to adaptive reorganization of the brain after injury. Figure 7*A*,*B* depicts the proportion of contralesional choices before (blue) and after (red) the PRR inactivation over the course of the control and inactivation sessions in the two monkeys. We assessed the effects of repeated injections on the choice bias by fitting a linear regression model to the data (Fig. 7*A*,*B*, blue line for control sessions, red line for inactivation sessions). The results showed a significant increase of contralesional choices over the period of successive injection sessions for monkey G (R-square = 0.6912, $p < 0.05$). However, a similar trend was also found in the control sessions for monkey G, although the increase of contralesional choices was not significant (R-square = 0.28, $p = 0.11$, not significant). On the other hand, we found no effect in the choice bias over the period of the re-

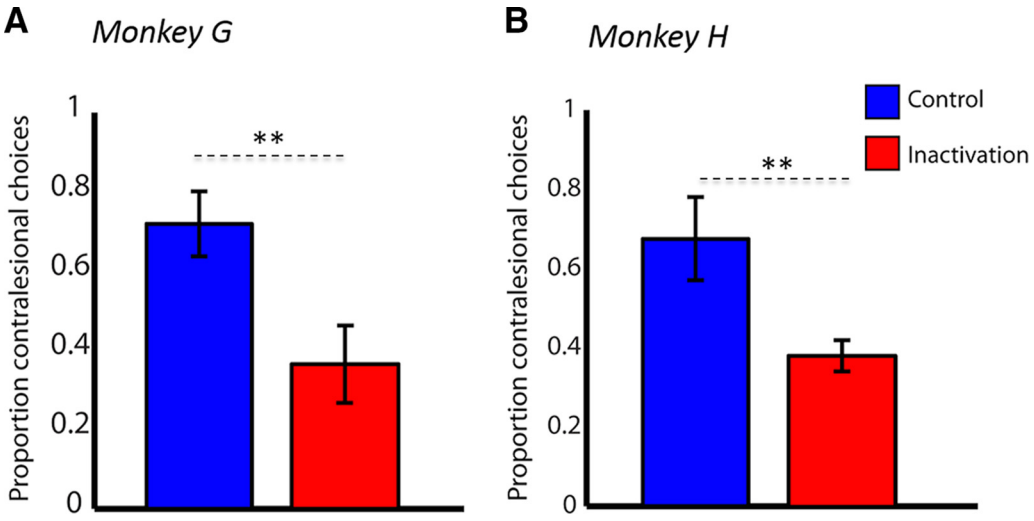

Figure 6. Proportion of reach choices toward the contralesional hemifield (free-choice trials) during control and inactivation sessions for monkey G (***A***) and monkey H (***B***). Notice the strong decrease of contralesional choices in inactivation sessions. The error bars indicate SD across all sessions. $^{**}p < 10^{-6}$ (10 and 8 control and inactivation sessions, respectively, for monkey G, and 10 and 7 control and inactivation sessions, respectively, for monkey H).

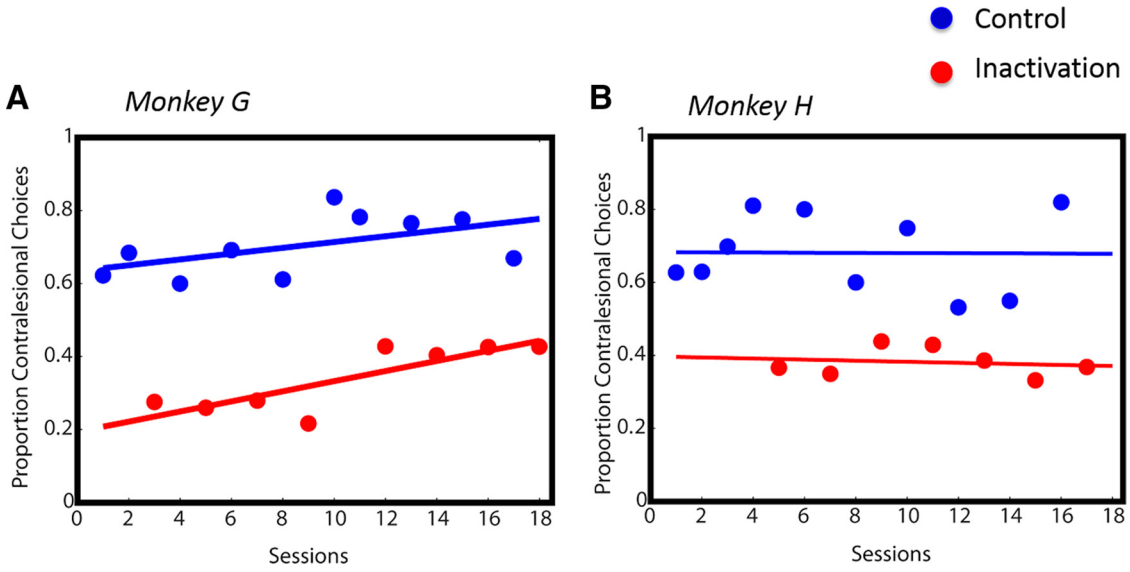

Figure 7. Proportion of reach choices toward the contralesional hemifield (free-choice trials) as a function of the order of control (blue) and inactivation (red) sessions for monkey G (***A***) and monkey H (***B***). The corresponding regression lines are shown by blue and red lines in the control and inactivation sessions, respectively. The results showed a significant increase of contralesional choices over the period of injections but only for monkey G (R-square = 0.6912, $p < 0.05$), but note that this effect was offset by the corresponding increase of contralesional choices in control sessions (R-square = 0.28, $p = 0.11$, not significant).

peated injection sessions for monkey H (regression analysis R-square = 0.0000406 and 0.0256 for control and inactivation sessions, respectively). Therefore, we cannot make strong conclusions about whether 7–8 reversible inactivation sessions are enough for the brain to start long-term adaptation to the "lesion" in PRR. Future experimental studies with more inactivation sessions are required to assess this question.

Inactivation effects on memory saccades

Although PRR inactivation altered the selection between two targets presented simultaneously in both hemifields, it is still unclear whether this choice bias was due to a decision deficit or an attention deficit caused by the inactivation. To address this issue, we need to test whether the choice bias is effector specific. We trained the animals to perform memory-guided saccades either to a single target (instructed trials) or to select between two targets presented simultaneously in the left and right visual field (free-choice trials). Similar to the reaching task, instructed trials were interleaved randomly with free-choice trials in every session. We ran six and four control and inactivation sessions, respectively, for monkey G and seven and six control and inactivation sessions, respectively, for monkey H. Control sessions always started with the reach task, followed by the saccade task. Similarly, every inactivation session that involved the saccade task started with memory-guided reaching movements for ~15–45 min to ensure that drug injection caused changes in reach choices, followed by the memory-guided saccade task. Note that the animals repeated the reaching task after finishing the saccade task in most of the sessions to insure that the muscimol did not lose any efficacy during the saccade trials. We found that reach choice bias before the saccade trials was not significantly different from the reach choice bias after the saccade trials. In particular, the proportion of contralesional choices before and after saccade trials was on average

0.3831 and 0.3908, respectively, for monkey G and 0.4215 and 0.4407, respectively, for monkey H (two-tailed t test on control vs inactivation across sessions separately for the first and the second block of reaches was significant at $p < 10^{-6}$ for both blocks and both monkeys). The results demonstrate that there was no weakening of muscimol efficacy in the course of the data collection (≤2 h after injection). Figure 8*A*,*B* illustrates the proportion of saccade choices to the contralesional targets in control sessions and after the inactivation for monkey G (*A*) and monkey H (*B*). The results show that drug injection did not alter the saccade selection between the two response options. Hence, the choice bias in reaches after PRR inactivation is an effector-specific bias in spatial decision making rather than a bias in spatial attention, which suggests that PRR is part of a network that is involved in reach decisions.

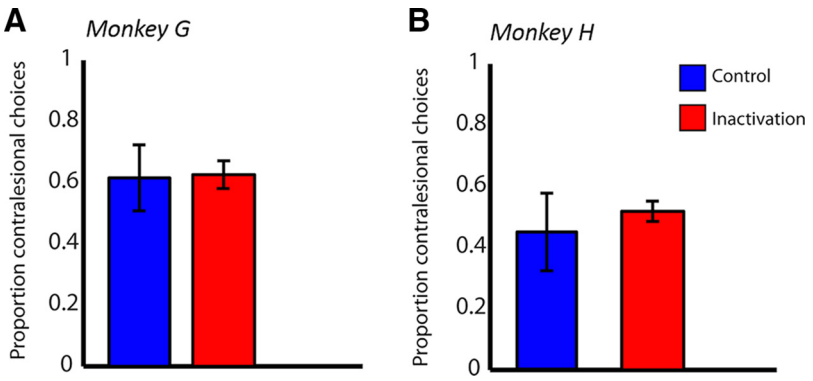

Figure 8. Proportion of saccade choices toward the contralesional hemifields (free-choice trials) during control and inactivation for monkey G (***A***) and monkey H (***B***). Notice that PRR inactivation did not affect the saccade choices. The error bars indicate SD across all sessions (6 and 4 control and inactivation sessions, respectively, for monkey G, and 7 and 6 control and inactivation sessions, respectively, for monkey H).

Discussion

The PPC is a classic association region involved in higher brain functions. Early studies of deficits from PPC lesions in humans led to the prevailing hypothesis that the PPC processes perceptual awareness, spatial perception, and attention (Bisiach and Vallar, 1988; Colby and Goldberg, 1999). This hypothesis is mainly based on neurological disorders occurring frequently after parietal lesions in humans, such as neglect and extinction syndromes. These syndromes are characterized by attentional deficits and impairments of perceptual awareness in the contralesional visual field (Mesulam, 1999; Kerkhoff, 2001). Recent studies provide evidence that the PPC is also involved in processing spatial information for a variety of cognitive functions, including movement planning (Andersen et al., 1997; Andersen and Buneo, 2002) and decision making (Platt and Glimcher, 1999). The main evidence is the existence of action-related (Mazzoni et al., 1996) and decision-related activity (Platt and Glimcher, 1999; Musallam et al., 2004; Scherberger and Andersen, 2007; Andersen and Cui, 2009) in specific areas of the PPC. However, it has been argued that the activity in the PPC is not "genuinely motor," but it is related to spatial attention and visual salience (Bisley and Goldberg, 2003; Padoa-Schioppa, 2011; Leathers and Olson, 2012).

All of these findings perpetuate a long-running argument about the functional role of the PPC in decision making. In the current study, we contribute to this debate by testing the hypothesis that the PRR is causally involved in internally guided reach decisions. To examine this hypothesis, we reversibly inactivated a portion of the PRR while two monkeys performed a delayed memory reaching or saccade task that included choices between equally rewarded targets. We found that both animals exhibited a spatial decision bias toward the ipsilesional targets after PRR inactivation, but only for reaching. On the contrary, the inactivation did not affect the saccade choices, nor did it impair the reaches and saccades to single targets in either hemifield. These findings cannot be explained as a spatial attention deficit, since the temporary "lesion" had an impact only on the reach choices, while leaving saccade choices intact. Therefore, PRR is part of a decision network for reach choices.

Our findings complement the results from a study conducted in parallel with our work, showing that PRR inactivation led to a reduction of contralesional choices in reaches but not in saccade choices (Kubanek et al., 2015). Despite the consistent conclusions of both studies, there are significant differences in the experimental procedures. Kubanek et al. used the double-target paradigm in a context of a stimulus onset asychrony (SOA) task with a variable delay between the onsets of the two targets. The animals had to select the target that appeared earlier to receive reward with 60% probability. This is a perceptual decision-making task rather than a free-choice task as used in our study. Additionally, the animals performed natural reaches (i.e., without a joystick), both reaches and saccades were immediate (i.e., without a memory delay), and the inactivation volume was smaller. The results showed that PRR inactivation led to a small reduction of contralesional choices only for reaches during both synchronous and asynchronous presentations of the two targets. Similar findings were also reported for saccade movements after LIP inactivation. Although these results are consistent with previous inactivation studies that used the asynchronous double-target paradigm (Wardak et al., 2002; Balan and Gottlieb, 2009), they differ from our findings as well as from those of previous studies (Wilke et al., 2012, 2013) that only used the free-choice and single-target instructed tasks—i.e., reduction of contralesional choices only when both targets are simultaneously presented. These findings and the direct comparison of inactivation effects on single-target trials within and outside of the SOA task (Wardak et al., 2002) demonstrate that the behavioral context (i.e., trying to correctly report the first target, as opposed to free choice between targets associated with equal and deterministic reward in our experiments) strongly affects the pattern of inactivation-induced deficits. Together, the results of our study and those of Kubanek et al. (2015) show that the PRR is involved in both perceptual (temporal order judgment) and internally guided, free-choice reach decisions, and the observed effector-specificity is not due to small injection volume or specific visuomotor contingency.

Action-based decision theory might explain the bias in reach choices after PRR inactivation

The consequences of PRR inactivation in choice behavior can be explained within the context of the action-based theory. This theory has been proposed as a complementary framework of the classic goods-based theory, which views decision and action as two separate and serial cognitive processes (Tversky and Kahneman, 1981; Padoa-Schioppa and Assad, 2006; Padoa-Schioppa,

2011). Alternatively, the action-based theory argues that goals have associated action plans and the decision emerges via a continuous competition between these plans (Glimcher et al., 2005; Cisek, 2007, 2012; Cisek and Kalaska, 2010; Rangel and Hare, 2010; Klaes et al., 2011). The main evidence for the action-based theory is the existence of decision-related activity in sensorimotor and other regions that have traditionally been related to planning movements. These findings led to the proposal that neurons in these regions integrate information from multiple sources (Gold and Shadlen, 2001; Sugrue et al., 2004, 2005). This information is used to bias the competition in the action-selection process.

We recently proposed a neurodynamical framework to model the computational instantiation of the action-based theory showing how the LIP and PRR can dynamically integrate information from disparate sources named relative desirability (Christopoulos et al., 2015). This value describes how "desirable" it is to move toward a particular direction with respect to the alternatives. A plausible scenario in the free-choice trials is that the relative desirability of each reach option is encoded by a population of PRR neurons with selectivity for the opposite hemifield. In the control sessions, the two targets provide the same amount of reward, but it seems that one of the reach actions has lower cost due to a lower biomechanical effort of reaching into the space next to the used arm. Therefore, reach actions to the contralesional hemifield are more "attractive" (i.e., higher desirability) than actions to the ipsilesional hemifield, leading to a choice bias toward contralesional targets in the control sessions. However, in the inactivation sessions, the muscimol injection decreases the relative desirability of the contralesional reach options (i.e., drug injection inhibits the PRR neuronal population that encodes the desirability of the contralesional reaches), resulting in a profound choice bias toward ipsilesional targets. The motivational underpinning of inactivation-induced spatial bias is supported by our recent inactivation study of the pulvinar (which is strongly interconnected with PRR), showing that the contralesional choice deficit can be alleviated by placing a large reward in the contralesional hemifield (Wilke et al., 2013). However, the action-based theory and the notion of relative desirability in the PRR provide just a theoretical interpretation of the results and further experimental work is required to validate the hypothesis. The current experimental set-up with equally rewarded targets does not allow testing whether PRR is integrating information from disparate sources to evaluate the alternative options. If PRR is part of a network for making reach decisions, then the effector-specific choice bias should be malleable to changes of reward and/or effort and/or aversion.

Relation to spatial extinction

Spatial extinction is a disorder occurring frequently after injury in the right parietal lobe in humans. It is characterized by the inability to perceive or react to contralesional stimulus but only when a simultaneous ipsilesional stimulus is also present. Despite many years of research, the pathophysiology of spatial extinction is still very much under consideration. The traditional view is that spatial extinction is caused by a selective attention deficit after parietal damage (Mattingley, 1999; Vuilleumier and Rafal, 2000). Our findings of effector-specific deficits argue against universality of this view. These spatial extinction-like symptoms cannot be explained as a deficit in general spatial attention or awareness, since the "temporary" lesion affected only reach choices.

Due to the differences in lesion etiology (e.g., stroke vs reversible inactivation), extent, and the different delays between lesion and measurement (days or months after lesion vs hours in the current study), a direct comparison between clinical work and our study is limited. More extensive neurological lesions might damage neural substrates of eye and hand action representations and thus result in more generalized deficits. However, our results provide evidence that in certain cases, spatial extinction is effector specific and thus it might represent a deficit in decision making rather than spatial attention. On the other hand, further experimental studies require assessing the mechanisms of spatial-specific and action-specific deficits. For instance, clinical studies have shown that motivational factors have an impact on spatial extinction behavior (Domínguez-Borràs et al., 2012). It would be interesting to explore whether the choice bias we observed after PRR inactivation is alleviated by increasing the reward in the contralesional hemifield.

Conclusions

To summarize, we reversibly inactivated the PRR while two monkeys performed memory-guided reaching or saccade movements. We found that PRR inactivation led to a pronounced choice bias toward the ipsilesional hemifield, but only for reach choices. Thus, the PRR selectively contributes to internally guided reach decisions.

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